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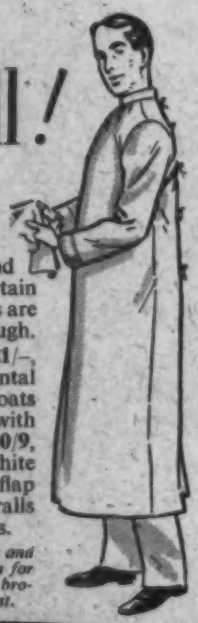

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BRITISH MEDICAL JOURNAL

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THE M'NAGHTEN RULES AND MODERN CONCEPTS OF RESPONSIBILITY*

BY

ELIOT SLATER, M.D., F.R.C.P., D.P.M.

Honorary Physician, Maudsley Hospital

[*In what follows the author has drawn from the Report of the Royal Commission on Capital Punishment; but responsibility for the views expressed is his alone.*]

We are nowadays becoming increasingly aware that there is such a thing as social pathology, and that there are diseases of the body politic which are not diseases of the individuals which compose them. This awareness has come to us through the study of individual psychology, of psychosomatic disorders, and disorders of interpersonal relationships. Many of the aberrations we observe seem to have been caused by no defect or disease of the individual sufferer, but by the fact that he was caught up in unfavourable circumstances, which themselves resulted from the nature of the society in which he lives. An obvious example is juvenile delinquency: a certain amount of delinquency is traceable to disorders and defects of the individual, such as mental deficiency and epilepsy; but in the majority of cases the failure seems to be mainly caused by social inadequacies, disturbances in home life, deficiencies in training, lack of normal outlets, and factors of such kinds.

It is useless to maintain that these social evils are no concern of psychiatry and should be reserved for the economist and sociologist. Their effects are constantly to be seen by the psychiatrist in his daily work; and those of us who believe that the State exists for the welfare of the individual must also believe that, from the study of individuals and the conditions in which they thrive or break down, general directives for the planning of social organization must also be derived.

It is against such a broad background that one best approaches the peculiar problems of criminal responsibility. For many years legal and medical views on this subject have been diametrically opposed. How is it, one may ask, that two groups of professionally trained minds have found it so impossible to understand one another that they can hardly enter a discussion together without unnecessary affect? How is it, with all the growth of knowledge of the working of the human mind, that we are still burdened with a doctrine of criminal responsibility which is more than a century out of date, while other civilized countries have progressed far beyond us? We are faced with an example of social pathology, and the history of the illness and the present status should prove interesting.

When in 1843 M'Naghten shot at and killed Sir Robert Peel's secretary, believing the man to be his master, his case was not decided by the M'Naghten Rules, nor was he found guilty of the act charged. These Rules and the form of the verdict in the case of insane killers were refinements introduced after his time. When it had been shown in evidence that M'Naghten suffered from a number of delusions of persecution, and that the killing had been inspired by these delusions, the judge did not even leave the verdict to the consideration of the jury, but directed them to find him not guilty. At that time Broadmoor did not exist, and, though by an Act of 1800 criminal lunatics had a special legal status, arrangements for their security and care were not, perhaps, very satisfactory. The public reaction could hardly have been greater if the killer had got off scot-free. It culminated in a debate in the House of Lords, where five questions were put to those of its members who were judges; and the replies of 14 of the 15 judges to the questions constitute the Rules.

The M'Naghten Rules

The answer to the first question states that persons who labour under partial delusions only, and are not in other respects insane, who know, moreover, that their act is contrary to the law of the land, are nevertheless punishable for that act.

The second and third questions were answered together, and constitute the M'Naghten Rules as we know them to-day. They state that every man is to be presumed sane, and to possess a sufficient degree of reason to be responsible for his crimes, until the contrary is proved to the satisfaction of the jury, "and that to establish a defence on the ground of insanity it must be clearly proved that, at the time of committing the act, the accused was labouring under such a defect of reason, from disease of the mind, as not to know the nature and quality of the act he was doing, or, if he did know it, that he did not know he was doing what was wrong." The answer goes on to say that the party's knowledge of right and wrong should be put to the jury with reference to the act charged, rather than generally. "If the accused was conscious that the act was one that he ought not to do, and if that act was at the same time contrary to the law of the land, he is punishable."

It is noteworthy that since the formulation of the Rules an element of increased rigidity has been introduced by subsequent decisions. The judges who formulated the Rules seem to have recognized the distinction between subjective right and wrong in the mind of an accused person and objective right and wrong as defined by the law of the land, and to have held the former to be the criterion. A man who believed that another was the incarnation of Satan, and that he was commanded by God to kill him, would seem to be excused by the

*A lecture given at Maudsley Hospital on December 9, 1953.

original formulation, though not by the Rules as they are administered to-day. A later decision in the Appeal Court has laid it down that if a man knows his act is against the law it is enough.

The answer to the fourth question states the extent to which a delusional belief may constitute a defence, in the case of persons suffering from partial delusions only and not in other respects insane. "We think," runs the answer, "he must be considered in the same situation as to responsibility as if the facts with respect to which the delusion exists were real. For example, if under the influence of his delusion he supposes another man to be in the act of attempting to take away his life, and he kills that man, as he supposes, in self-defence, he would be exempt from punishment. If his delusion was that the deceased had inflicted a serious injury to his character and fortune, and he killed him in revenge for such supposed injury, he would be liable to punishment."

The answer to the fifth question is of no interest, as it merely defines the circumstances under which a medical witness, who has heard the evidence in court, may give evidence about the responsibility of the accused.

The judges were called on to state what the law was in 1843, and not what the law should be. The effect of their ruling was such that M'Naghten himself would have been otherwise judged than he had been. The state of public opinion at the time was such as to demand a tightening up of the law, and this is a thing which lawyers are never loath to do. Nevertheless the effect of the Rules has been to stabilize the law at the time of 1843 into being the law of the country for all time. This is an event without equal in the history of English common law. For the law of murder is common law, and not statute law, and the common law is a growing organism. With the M'Naghten Rules that branch of the common law which relates to the criminal responsibility of mentally abnormal persons was suddenly frozen, and all further growth and development were prevented. In the interval the world has changed almost beyond recognition; psychiatry has grown from infancy into adolescence. But the law has stayed where it was. It has learned nothing and it has forgotten nothing.

The question why this has been so is interesting. In themselves the M'Naghten Rules have no authority. Even now it is only the answer to the second and third questions that has the force of law. The Rules were made in the abstract, as it were. The judges were not called on to exercise any recognizable judicial function, and were speaking merely as theoretical experts. The authority of their Rules was, in itself, no more than the authority of a textbook or treatise on the law. All the authority the Rules now have has been given to them subsequently in actual cases to which they have been applied.

Discontent with the Rules

Medical men have never been content with the Rules, even at the time of their formulation, and have constantly striven against them. But even lawyers have found them unsatisfactory. The most notable of these lawyers was undoubtedly Stephen, who eighty years ago had a better understanding of the nature of mental disease and the way it might affect responsibility than most of his present-day colleagues have now. The doctrine, that a delusional idea should excuse only that which it would also excuse if the idea were true in fact, he exposed for the nonsense it is by pointing out that the evidential value of a delusion is that it is "in all cases the result of a disease of the brain, which interferes more or less with every function of the mind, which falsifies all the emotions, alters in an unaccountable way the natural weight of motives of conduct, weakens the will . . ." Stephen tried to introduce a way of interpreting the Rules which would bring them into conformity with clinical facts, but he was not successful. In course of time the interpretation of the Rules, in those cases in which they are specifically applied, has become stricter rather than more liberal; and their correct interpretation has now become very rigid indeed.

Their Clinical and Forensic Consequences

For a man to be excused, on the ground of insanity, for a criminal act of any kind he must be so mentally diseased that he either does not know the nature and quality of his act or does not know that it is wrong. "Wrong" means "against the law of England," and not against the law of God or against the moral convictions of the actor. Not knowing "the nature and quality of the act" has also been clearly defined; it means to be grossly mistaken about the physical nature of the act. In the words of Mr. Justice Cassels in the Straffen trial: "If a person was charged with having manually strangled some person, and the jury was satisfied that when he strangled that person he thought he was squeezing the juice out of an orange, that would be a failure to know the nature and quality of his act."

No one, doctor or lawyer, has disputed that, in the strict interpretation of the Rules, such as is alone sanctioned by the law, the great majority of insane people are not insane enough to come under their dispensation. From the clinical point of view only those are "M'Naghten mad" (to borrow a useful phrase from Dr. Desmond Curran) who are suffering from a gross disorder of consciousness, such as is seen in a post-epileptic twilight state, an organic delirium, or the gravest degrees of dementia or mental defect. The conscience of the medical man is affronted by the suggestion that the melancholic woman who kills her child, the paranoid schizophrenic who kills his imagined persecutor, should be regarded as responsible for acts which are the immediate consequence of their illness.

This attitude is universal among medical men. Those psychiatrists who support the modern application of the M'Naghten Rules do so on the ground that they work, or are made to work, so as to conform with our ideas of justice, that, in fact, they are not so strictly applied as to exclude the melancholic or the schizophrenic.

The discontent of medical men with the M'Naghten Rules has not been generally shared by men of law. Nearly all of the judges and lawyers who gave evidence to the recent Royal Commission on Capital Punishment were against any modification of the Rules and wished to see them retained as they were. The lawyer's attitude to the Rules was stated pithily by Lord Bramwell in 1874, in opposing a draft Bill drawn up by Stephen. His phrase has deservedly become immortal. "I think," he said, "that, although the present law lays down such a definition of madness, that nobody is hardly ever really mad enough to be within it, yet it is a logical and good definition."

Arguments Against Modification

The principal arguments which have been advanced by lawyers against any modification of the Rules can be briefly stated. Rules of some kind are necessary, it is said, because without the guidance of rules the jury would be fumbling in the dark or would become entangled in a mesh of psychiatric verbiage. If rules there must be, then these Rules are as good as any; and it is found easy to point out many and grave defects in any modification which anyone is so rash as to try to set down in precise terms. The weight which should be given to these arguments is very doubtful. There is, for instance, reason to think that when juries retire to consider the responsibility of a mentally abnormal accused person they do in fact address them-

selves to the question whether or not he is insane, in the ordinary lay sense of the term, and then, if they think he is, decide that he must therefore come within the Rules, whatever those Rules do in fact say.

However, the arguments advanced by lawyers in support of the Rules do not seem to be as important as the motivations which suggest them. The insane person who is legally not responsible for his criminal act and is excused thereby from suffering the consequences is a privileged person; and it is natural and proper that lawyers should feel that privilege of this kind is an anomaly, essentially highly undesirable, and that the class of those who benefit from it should be as narrowly and strictly limited as possible. From this point of view it is to some extent irrelevant that an insane criminal is not immune to the consequences of his criminal acts, but suffers consequences different in kind from those which fall to the lot of responsible people. In the case of murder, the privilege of escape from death, even though the alternative is to be immured for life, is still felt to be so very great that it offends against the idea that all persons should be equal before the law. If this country were once to abolish the death penalty, then the anomalous privilege would cease to exist; and I think the attitude of lawyers would become a very different one.

It is from their different motivations that the conflicts between medicine and the law, which are such an obnoxious feature of many criminal trials, arise. The medical man is by the nature of his profession predisposed to aid the sick man, to secure recognition for his illness and its consequences, and to defend him from the reproach that abnormalities of behaviour caused by illness are to be attributed to wickedness. The lawyer looks at matters very differently; and for him the ideals of justice and of equality between man and man before the law are paramount.

From the lawyer's point of view there are great advantages in having rules which are narrow and strict. By their means one can be almost sure of preventing any particular person from successfully claiming non-responsibility, if one so wishes, whatever the evidence may be. Sir Norwood East, a forensic psychiatrist of the greatest experience, and a warm supporter of the Rules, put it this way in his evidence to the Royal Commission: "If the judge is perfectly satisfied in his own mind that the man is insane, he is quite likely to stretch the M'Naghten Rules, and does stretch them so far that they may not be used at all . . . but . . . judges were ready to apply the M'Naghten Rules strictly if there was in their opinion doubt or reason to think that the person was not insane." That this was the general practice was confirmed by all other witnesses with court experience.

Administration of the Rules

This is how the matter now stands. In the majority of cases which come before the courts the M'Naghten Rules are a dead letter; in a minority of cases they are applied in their full rigour. Notorious cases, in which much public feeling was aroused, and in which they were strictly applied, are the cases of Heath, Haigh, and Straffen. The person who decides whether the Rules shall be applied strictly, loosely, or not at all is the trial judge. If he applies the Rules strictly in his summing up to the jury, and in consequence a lunatic is found to be responsible, the lunatic and his legal representatives have no redress, other than through the administrative action of the Home Secretary. No appeal to a higher court will help, as the Court of Appeal is bound by the law and its own previous decisions to support the strict application of the Rules made by the trial judge. If, however, the judge does not apply the Rules, or only applies them loosely, then if the defence of insanity succeeds there will be no appeal, no review of his summing-up, and if it fails the accused will have no reason to complain of the lenience with which the Rules were applied. This is, of course, a very satisfactory position for judges, as it amounts to a sort of "heads-I-win-tails-you-lose." In borderline cases it permits them to make reasonably sure that only those persons "get off" (as the lawyer calls it) who they think should get off. But for others, who have less confidence than the judges in the reliability of their opinions about who is and who is not insane, the position is less satisfactory.

Apart from the criticisms which can be made of the Rules themselves, grave complaint may be made of the method of their administration.

1. They are inequitable as between case and case. In the cases of some wrongdoers they are applied rigorously, in the cases of others loosely or not at all. Some mentally abnormal persons have their responsibility adjudged by different standards from those which are applied to others.

2. They are inequitable as between judge and witness. The judge is free to ignore the Rules if he so wishes, but if he so wishes he can always tie the medical witness down to them as strictly as he likes.

3. By applying or not applying the Rules in his directions to the jury the judge can exercise a large measure of control on the jury's decision. The judge, and not the jury, becomes the arbiter on what is supposedly a matter of fact.

4. The Rules are not applied candidly. If the work were to be done candidly, the judge would point out to the jury that "nobody is hardly ever really mad enough" to be covered by the Rules, and that, by that standard, the great majority of patients certified insane and permanent inmates of mental hospitals would be regarded as responsible. Once juries grasped this fact they would draw their own conclusions.

Influence on Psychiatric Evidence

The worst effect of the Rules from the medical standpoint has still to be mentioned. This is their influence, in disputed cases, on the way in which psychiatric evidence is taken and the medical witness is examined and cross-examined. As the only thing that matters is whether or not the mental abnormality of the accused passes the M'Naghten test, the really important clinical aspects get passed over. No attempt is made to show in any detail in what way the accused was mentally abnormal, or what was the significance of the abnormality in the chain of cause and effect which led to the crime. The judge's summing-up in the Straffen case shows to what lengths the law goes in assigning relevance to what are, from the medical point of view, trivial, insignificant, or even wholly metaphysical and speculative aspects of the case, and to what extent the dynamics of the crime are dealt with as irrelevant. The facts in the Straffen case need only the briefest recapitulation. The killer was a feeble-minded youth who, on the occasion of a previous murder, had been found unfit to plead because of his mental deficiency. Some years later he escaped from Broadmoor, where he had been confined, and in a few hours of liberty committed another murder.

On this second occasion he was found fit to plead, and the question arose at his trial whether he was medico-legally responsible. In his address to the jury Mr. Justice Cassels said: "Ask yourselves whether you are satisfied by the defence that at the time when he did that murder he was insane within the meaning of the criminal law; not that he was feeble-minded; not that he had a lack of moral sense; not that he had no feeling for his victim or her relatives; not that he had no remorse; not that he may be weak in his judgment; not that he fails to appreciate the consequences of his act; but was he insane through a defect of reason caused by disease of the mind, so that either he did not know the nature and quality of his act, or if he did know it, he did not know that it was wrong?"

The fact that such an attitude is the one required by the law prevents the proper presentation of psychiatric evidence; it impedes scientific advance in the understanding of the relation between mental abnormality and crime; and it throws a barrier in the way of education of the public and of officers of the law in what our scientific knowledge and understanding already are. This is the lesion in social organization to which the curious concatenation of events which followed the M'Naghten case has now led.

Let us see how far we have arrived with the analysis of a specimen of social pathology. In 1843 the common law was evolving by its natural slow process of development. However, knowledge of insanity was very rudimentary, and the fear of madness and the mad much greater than now. There was also then no great public assurance that a non-responsible killer was automatically rendered socially innocuous. A horrifying murder focused public attention on a largely illusory danger. The public response was, of course, emotional and irrational, and was directed against persons rather than organizational defects. What amounted to legislation, though it was not recognized as such, was completed in a hurry, without considering what was the real nature of the problem. A solution of the wrong problem having been found, it was imposed, and became a kind of permanent splint on a growing structure. Having once been imposed, vested interests grew up to keep it in place. Its effects are to mete out an unequal justice, to prevent honest and unemotional inquiry, and to prejudice the relations between medicine and the law.

Other Countries

An essential part in studies of pathology is played by the control case. We have seen where we have been taken in this country; how have they got on in other countries where there was no M'Naghten and there have been no M'Naghten Rules? The nearest country at hand is Scotland. In Scottish law, the M'Naghten Rules have exerted a certain effect, in directing the way in which judges will ask juries to decide the responsibility of an accused person; but in the important group of homicides the whole position is transformed by the existence of the doctrine of diminished responsibility. This doctrine is particularly suitably applied to the borderline cases which in English law cause so much difficulty. The doctrine of diminished responsibility has arisen over the course of 100 years by a process of natural growth in the common law and depends on no statute. In answer to a charge of murder the accused may put forward a defence of diminished responsibility and will then be called on to prove that, though not insane, he yet suffered from mental weakness or abnormality bordering on insanity to such an extent that his responsibility was substantially diminished. Mental deficiency, post-traumatic personality change, even a severe neurotic state, may be adequate medical grounds to substantiate diminished responsibility.

By a recent decision psychopathic personality, by itself, has been held to be insufficient. If the jury find the responsibility of the accused was diminished in this way, then he will be found guilty not of murder but of culpable homicide, and will be sentenced to imprisonment for a period, usually several years, which is decided by the judge. In practice this law is found to be very effective and is strongly supported by all Scottish lawyers. Although there is no arbitrary system of rules, such as the M'Naghten Rules, to help the jury to decide whether or not responsibility is diminished, it is said that juries find no particular difficulty in deciding one way or the other.

The doctrine of diminished responsibility has also found its way into the legal systems of other lands—India and Pakistan, Western Australia, South Africa and Southern Rhodesia, and certain of the United States of America. In these countries diminished responsibility will suffice in some for a sentence of life imprisonment instead of a sentence of death, or for the recording instead of the pronouncing of a sentence of death, or for a recommendation for mercy from the jury, or for reduction of the degree of murder from first to second degree.

In no other European countries than our own is any legal definition of the degree of insanity which shall exclude responsibility found necessary; and the decision whether the mental abnormality of the accused was sufficient to relieve him of the liability to punishment is in effect left to the jury to decide on medical and other evidence.

In the Scandinavian countries forensic psychiatry presents an altogether different picture from that in the English-speaking world. In Sweden, for instance, evidence on the psychiatric aspects of a crime is given almost exclusively by specialists in the service of the State. Psychiatrists act as counsellors in the courts—that is, as subsidiary judges and aids to the trial judge himself. The courts may ask for a psychiatric examination of the accused, not only if it is suspected that the crime was committed in a mentally abnormal state, but also if medical evidence is needed to help decide what penal treatment would be the most appropriate. No legal definition of psychiatric non-responsibility is used as a yardstick, and, quite simply, the perpetrator of a crime is excused from punishment if the crime was committed under the influence of psychosis, or mental deficiency, or another mental abnormality of such a fundamental nature that it must be considered to be on a par with psychosis.

Thus the severer sequelae of brain injuries, encephalitis, etc., and very severe forms of psychopathy will be so considered, especially if they have already in the past interfered with a normal social life; for instance, by causing repeated admission to a mental hospital. The very concept of non-responsibility is hardly taken into account, the real grounds for excusing a man from punishment being that, in his case, punishment is an irrational method of treating him, his proper treatment, whether therapeutic or solely custodial, being best left in medical hands. The administrative method of dealing with such cases is not different from that employed for other patients who are a social danger but have not committed crimes, and admission to an ordinary and not a special criminal psychiatric hospital is the mode of disposal.

What is true of Sweden is also largely true of Denmark and Norway. Capital punishment does not exist in these lands, which means that conflicts between legal and medical viewpoints in an acute form and with maximum publicity do not occur. Medical opinion almost always prevails in the courts, but its effect is often to add to any sentence of punishment, which may itself be reduced on psychiatric grounds or wholly omitted, a further period of subjection to safety measures. The effect of this is greatly to diminish the enthusiasm with which the defence will be inclined to seek for psychiatric examination. The psychotic subject is not sentenced to any form of punishment, but will be sent to a hospital. Psychopaths tend to be regarded as responsible for their acts, but may be subjected to safety measures in lieu of or in addition to any punishment.

The Meaning of "Responsibility"

In Scandinavia, therefore, we arrive at the opposite pole from that at which we are placed in this country. The pragmatic solution of the question, "What are we to do with this man?" is regarded as the important task, rather than the theoretical solution of the question, "How are we to adjudge this crime?" This brings us to the important problem of what it is we mean when we talk about "responsibility."

For the English lawyer the meaning of the word is clear. For the lawyer "responsible" means only "liable by the law of England to be convicted and punished for a criminal act." This meaning is, for our present purposes, entirely useless, as it is entirely arbitrary. What we have to do is to decide whether any scientific meaning can be given to the word "responsible." As the ordinary man uses the word, an ethical judgment is implicit, and what he really means is that a "responsible" man is one whom one can properly hold responsible, whom one can call to account for his acts.

To the mind of the ordinary man, the lunatic is certainly non-responsible, and the average healthy citizen is as certainly responsible. Doubts and difficulties arise, however, when the mentally abnormal but not grossly insane individual is considered. Furthermore, we may usefully ask

whether the insane patient is to be regarded as non-responsible for all his acts. Is he non-responsible when he cleans his teeth in the morning instead of at night before he goes to bed? Is he to be regarded as responsible if he resolutely refuses to have his brain damaged by leucotomy? And is the normal man always to be regarded as responsible? As a case in point, when he cowers whimpering at the bottom of a trench when he has received the order to advance under fire? Is it in conformity with our principles of justice to sentence such a man to imprisonment for cowardice?

If medical men are to be required to give evidence about diminished responsibility it would be possible to use the concept of causation to help the ends of justice. If it seemed that illness or defect or disease had entered as a material element into the causation of the crime, there would be so much reason to regard responsibility as diminished. Even then there would be difficulties. In the case of Raven, who butchered his parents-in-law, there were strong reasons for regarding him as epileptic, but the crime could be interpreted as a cold-blooded one, motivated on the desire for material gain. Unless we are to take the stand that the whole personality is involved in every crime and that any existing abnormality is inevitably involved in its causation, we are liable to land in difficulties, and be called on to make decisions which are bound in some degree to be arbitrary.

Finally, how are we to regard the psychopath? If defects of intelligence are to be allowed weight, are we justified in excluding defects of personality? Is there any satisfactory distinction to be made between the psychopathic criminal and the criminal of bad character? When giving evidence before the Royal Commission the prison medical officers were asked to say what was the difference between a "thug" and a psychopath; and the answer came, "A thug is a thug because he wants to be a thug; a psychopath cannot help it." I confess myself that I cannot see either the force or the practical usefulness of this distinction. Can the thug help wanting to be a thug? And is the man who does a deed of shame to be regarded as abnormal if he subsequently regrets it, but to be regarded as normal and a criminal if he subsequently glories in it or views it with indifference?

An Unscientific Approach

These considerations lead one to the view that attempts to measure the responsibility of others are essentially unscientific. There is nothing objective about the idea which could possibly provide a standard of measurement. Even as a value judgment, responsibility offers extraordinary difficulties. I suspect that when we give opinions about the responsibility of others we are really reporting on our own states of mind. Perhaps we are doing little more than identifying ourselves with the criminal and asking ourselves whether or not we could have been guilty of his crime. If we then feel that we could have done it only after going mad, we may give one sort of answer; if we feel that we could have done it, but only by suppressing the whole of our better nature, then we shall give another sort of answer. Responsibility, it is worth noting, does have some meaning subjectively, in our judgments on our own actions. It is only when we apply the concept to the actions of others that it breaks down.

No theory of mental medicine could develop without the working hypothesis of determinism. When a man acts in a given way at a certain time under a particular set of circumstances we must assume, if we are going to understand his conduct at all, that it was determined by such things as his own make-up, his physical and mental state at the time, and the circumstances and his appreciation of them. The "free will," on which both law and religion are based, proves a heuristically sterile idea. If we attempt to inject it into our analysis of causation it only introduces an element of the unknowable. If we are to inquire at all we must assume that the processes of inquiry will eventually enable us to answer the questions we put; and we are precluded from supposing that there are decisive causes, producing observable effects, which are for ever beyond the reach of inquiry.

Now if every act which a man performs is determined by his own nature on the one side and circumstances on the other, then no other way of acting was open to him. The application of such concepts as responsibility, innocence, and guilt becomes nonsensical. In psychiatry we do very well without them. It may be important to discover whether a patient feels guilty, but we find no need to say, ourselves, he is guilty. If we refrain from making use of such judgments of value, not only is it easier to understand our patient's behaviour, and to predict what that behaviour will be in future circumstances, but our personal rapport with the patient is easier too.

This is the point at which the Scandinavian system has arrived. The whole idea of responsibility, even the idea of diminished responsibility, is there gradually dropping out of use as being unnecessary for practical purposes. The question is asked instead, will the criminal be benefited by punishment?

Punishment

This brings us to the questions what is punishment, and how is it justified. Punishment, I take it, consists in making special arrangements to secure that certain modes of behaviour shall be succeeded by disagreeable consequences. Its corollary is the provision of rewards for desired behaviour. The two together are merely a way of conditioning stimuli, a procedure which is valuable, even necessary, in the training of animals and children as well as of adults. The aims of punishment are often said to be deterrent, reformatory, and retributive. The first two of these three are clearly connected with training, and justify as pragmatically useful the application of punishment to non-responsible as well as responsible beings. Something quite different is involved in retribution.

Retribution seems to involve the idea of making a payment. Its justification is purely emotional, and has a basis in the group psychology of the society which requires the payment and the individual psychology of the offender who has to make it. There seems to be an emotional need for it on both sides, and an equally emotional feeling that, once punishment has been undergone, the ill deed has been wiped off the slate as it were, and can be forgotten. The retributive element in punishment is very often condemned by rationalists; but it must not be forgotten that it is the element which balances offences with appropriate punishments, and will not permit an excessive punishment for a minor misdeed. It is in regard to our feeling that the non-responsible person should be excused retribution, that responsibility becomes important for justice.

How, then, are we to reconcile these antagonists, the line of thought that teaches us that responsibility is almost meaningless from an objective viewpoint, and the thought that shows that some people are to be dealt with differently from others? A compromise might be made along the following lines.

Abnormality of Crime

Statistically, crime is abnormal in the sense of being unusual. For it to occur there must have been something unusual either in the criminal or in the circumstances which motivated the crime. If a man finds half a crown on the floor of his office, picks it up, and keeps it, what is statistically unusual is the combination of circumstances. The man himself is not particularly likely to be unusual; in fact, it is the man who would make some effort to find the loser who would be the unusual one. The great majority of minor offences—trying to smuggle some trifle through the customs, riding a bicycle after dark without a light, and so on—are of this kind. It would be highly uneconomic, in the application of deterrent measures, to bother oneself about the possible abnormalities in the wrongdoer. He may be adjudged as average, and subjected to the procedure appropriate to the average case. If, however, we find that X is now being tried for his thirtieth offence of

indecently exposing himself, the evidence is overwhelming that it is not the circumstances which are unusual but the man. We might then very properly apply the Scandinavian system of trying to say what is the best way of handling the man, and abandon methods of treating him which would be appropriate only to the average case.

What is so obviously true of the recidivist criminal may also be very often true of the single very abnormal crime. Murder, in the statistical sense, is highly abnormal; in England and Wales there are only about 150 murders a year. Murder is also in a majority of cases the act of a man who is mentally ill. In this country, over the course of fifty years, in 22% of murders known to the police the suspect committed suicide. Of murderers brought to trial at Assizes, 14% were found unfit to plead. Of those found guilty of the act charged 39% were found guilty but insane. Of those sentenced to death 4% were respited to Broadmoor, and a further 42% had their sentences commuted to penal servitude, in a proportion of cases on psychiatric grounds. It is then hardly surprising that no one has been able to produce any convincing evidence that capital punishment acts as a deterrent for such a pathological event.

Conclusion

At the present stage in the development of criminal law, we are half-way between the irreconcilable aims of fitting the punishment to the crime and fitting the punishment to the criminal. It would not seem possible to abandon either aim entirely and replace it by the other. But it should not be beyond the reach of inquiry to find the principles of classification which would provide the basis of a just and efficient penology, to find the means of distinguishing the crimes in which the element of personal deviation is large from those in which it is small, to classify the kinds of deviation and measure their degree, and to work out the means of treatment of the causes, both in individuals and in societies, which lead to crime.

TREATMENT OF PERIPHERAL VASCULAR DISEASE IN OLD AGE*

BY

E. J. WAYNE, M.D., Ph.D., F.R.C.P.

Regius Professor of Practice of Medicine, University of Glasgow

With increasing age the incidence of atherosclerosis rises, and more old people die from the resultant occlusion of an important blood vessel than from any other cause. Information about the incidence of a significant degree of atherosclerosis is difficult to obtain, but when the peripheral arteries of the legs are involved a definite symptom, intermittent claudication, may arise and can be recorded. Gavey (1949) found that this symptom was present in 1.1% of 360 persons over the age of 70. Droller and Pemberton (1953) encountered it in approximately 6% of "elderly" people, although it was disabling in only 1.5%. Since, however, this complaint will usually arise only in those able to walk far or fast, it is probable that an even larger number of old people have a diminished blood supply to the lower limbs. In many who are admitted to hospital for other reasons, examination will reveal cold feet, nutritional changes, or absent pulses at the ankle. Some may present with gangrene. Old people, moreover, take less exercise, are often confined to bed, and may suffer from bouts of congestive heart failure. They are thus especially liable to develop venous thrombosis. The prevention and amelioration of these consequences of peripheral vascular disease in the elderly are clearly important problems.

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Aetiology of Atherosclerosis

This vast and controversial subject is discussed only so far as it is relevant to the possible prevention or improvement of the pathological state which underlies peripheral arterial disease. The condition known as senile medial calcification (Mönckeberg's sclerosis) is of little interest in this connexion, as it leads to rigidity but not to narrowing of the arteries affected. Atherosclerosis is found with unexpected frequency in conditions associated with hypercholesterolaemia, such as diabetes, myxoedema, nephrosis, and essential familial hypercholesterolaemia. Gofman (1951) has shown that the serum cholesterol is bound to protein and that the lipoprotein molecules vary in size. By using the ultracentrifuge, he has been able to demonstrate that patients with diseases predisposing to atherosclerosis and those who have suffered a coronary thrombosis have present in their blood serum a relatively unstable lipoprotein molecule. Its relative concentration can be reduced by dietary restriction of cholesterol and fats.

Isotope studies have shown that some of the cholesterol present in the blood is derived from the acetate residues which result from normal fat, carbohydrate, and protein metabolism. It seems likely, therefore, that it is not only the cholesterol content of foodstuffs which is important but also the total calorie intake. There is strong supporting evidence that a high dietary intake of fat is linked with atherosclerosis, and there is some evidence that lipaemia is a factor in the causation of thrombosis. Duguid (1954) has, however, shed doubt on the association of the most important consequence of atherosclerosis—namely, arterial narrowing with a high cholesterol intake. Once symptoms due to atherosclerosis have developed it is in any case probably too late to advise dietary restriction, but it would nevertheless seem wise to recommend a low-fat diet to the elderly and the obese.

Kountz (1951) has claimed that advanced atherosclerosis is frequently associated with evidence of *hypothyroidism* and that the administration of thyroid extract is accompanied by a decrease in the incidence of the manifestations of atherosclerosis. There is little evidence to support this view, but it is probably true that mild hypothyroidism in the elderly is easily overlooked and may be a predisposing factor in arterial degeneration.

It is of the greatest importance to detect *diabetes mellitus*. The symptoms of this disorder in the elderly are often unimpressive, and patients may be seen for the first time with a gangrenous extremity. The disease is known to increase the rate of progress of atherosclerosis at all ages and it probably also gives rise to specific vascular changes which Lundbæk (1954) has termed "diabetic angiopathy." A high proportion of elderly diabetics suffer from occlusive vascular disease of the lower extremities. Lundbæk detected its presence in 50% of diabetics over the age of 60 and Semple (1953) in 42% of 100 diabetics with a mean age of 63. Of 52 consecutive cases of gangrene admitted to medical and surgical units, about half suffered from diabetes mellitus. Since the typical lesion is in the smaller vessels, gangrene in these patients can usually be treated conservatively and high amputation is rarely justified.

Clinical Features of Obstructive Arterial Disease in the Elderly.—The symptoms and signs of a diminished blood supply to the lower limbs are essentially the same at all ages. Their relative frequency, however, differs. Thus a young vigorous patient suffering from thromboangiitis obliterans is far more likely to complain of intermittent claudication than an old man whose capacity for exercise is limited by osteoarthritis or angina of effort. These patients are often admitted to hospital with the signs of thrombosis in a main artery or with small necrotic patches on the toes or heels. Usually they give a long history of persistently

cold feet. If old people are questioned on this specific point and the legs are examined, a comparatively large number will be found to have other signs of diminished blood supply. A further group have symptoms of "erythralgia"; they complain of burning pain in the feet which is worse when the feet are warm or dependent, and some are kept awake by "pins and needles" or by painful cramps.

Treatment

Treatment of the established condition of senile obstructive arterial disease is directed towards (1) the prevention of skin lesions and of gangrene by the avoidance of trauma, (2) the improvement of the blood supply to the tissues, (3) the relief of symptoms, and (4) the management of established gangrene.

Prophylactic Measures

Patients should be told that they must treat their feet as if they were valuable pieces of porcelain. It is better to give a leaflet with written instructions and to go through its contents with either the patient or a relative or preferably both. Instructions such as the following should be included:

Care of the Feet

1. Treat your feet with the utmost care. Avoid crowds.
2. Wash the feet daily with soap and warm water, dry well and rub in toilet lanolin. Apply talc powder between the toes.
3. Keep the feet as warm as possible but do not apply direct heat. Do not sit too close to the fire. Use warmed bed socks in bed but do not use a hot-water bottle below the thighs.
4. Wear warm clothing in winter and warm woollen socks.
5. Wear well-fitting shoes of soft leather with leather soles and do not wear new shoes for too long at a time.
6. Do not wear tight garters or sit with your legs crossed.
7. Cut the toe nails only after washing the feet. Cut them straight across.
8. Do not cut corns or use corn cures. Do not put strong antiseptics such as iodine on your feet.
9. Go to your doctor at the first sign of a blister, an infection, ingrowing toe-nails, or trouble with bunions or corns.
10. Preferably stop smoking altogether. If you cannot, smoke as little as possible.
11. Do the following exercise. Put a chair on the bed upside down so that its back can be used to support your legs, and put a pillow on it. Lie on the bed with your feet raised on the chair for two minutes. Lower the legs and lie flat on the bed for three minutes. Repeat four times. Do these exercises four times a day in a warmed room.

Attempts to Improve the Blood Supply to the Tissues

The blood supply to muscles is largely independent of nervous control and is determined chiefly by the local release of metabolites. The supply to the skin, on the other hand, is regulated chiefly by the sympathetic nervous system. It is therefore easier to devise methods of improving relative ischaemia of the skin than of the muscles.

The results of attempts to improve *intermittent claudication* are most disappointing. Hamilton and Wilson (1952) investigated the results of eleven different types of treatment over a prolonged period, as well as the effects of single administration of seven different drugs. The vast majority of 40 patients failed to show any improvement as the result of treatment. These observers point out the great difficulty which exists in assessing the results of treatment, as considerable fluctuations in exercise tolerance occur spontaneously. Fig. 1 shows an example of spontaneous improvement while a patient was receiving inert tablets. The increased exercise tolerance in such cases may be either psychogenic or, more probably, the result of the progressive improvement which sometimes follows an arterial obstruction while a collateral circulation is developing. Fig. 2 shows the difficulty in assessing the immediate effects of drugs. In this instance the improvement in exercise tolerance which followed the injection of saline would have been attributed to tolazoline ("priscol") if the control injection had been omitted. Whenever pain is "measured" it must not be forgotten that the figure is an index of a subjective phenomenon and as such may be strongly influenced by suggestion.

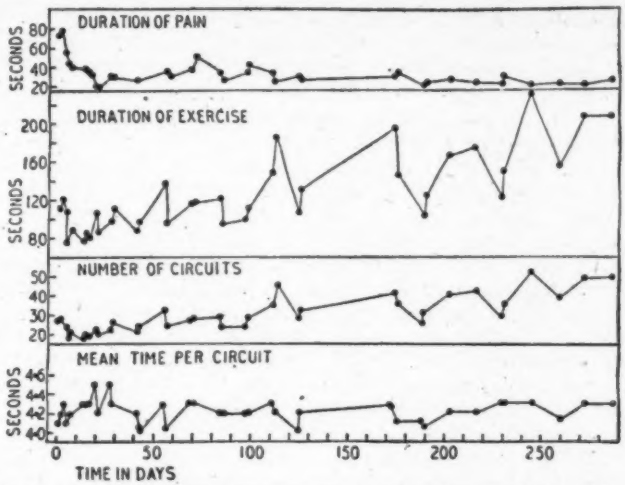

FIG. 1.—Spontaneous improvement in a patient aged 51 with intermittent claudication while receiving inert tablets for 300 days. The improvement is shown by an increased capacity to take exercise and a decreased duration of pain. The rate of walking (mean time per circuit) did not alter significantly (reproduced, by permission, from the *Quarterly Journal of Medicine*, 1952, **21**, 169).

A more complete investigation of the effect of natural vitamin E on intermittent claudication has been reported by Hamilton *et al.* (1953). Using the "double blind" technique, in which neither patient nor observer is aware of the nature of the substances tested, they found no appreciable difference in the response between vitamin E and arachis oil.

Attempts to improve the *blood supply to the skin* and subcutaneous tissues are more successful. Among the simplest is the reflex dilatation of the blood vessels which results from raising the general body temperature. The legs may be exposed. Buerger's exercises may help, although I suspect that reported beneficial effects are largely produced by psychological mechanisms. They are described above in a simple form as item 11 of "Care of the Feet." Vasodilator drugs have been used with varying success. Nicotinic acid (50 to 100 mg. three times a day) can be tried. Tolazoline is probably more effective. Goodwin and Kaplan (1951) recorded increased blood flows to the limbs of patients suffering from occlusive vascular disease as judged by observations in reflex heating tests and circulation rates. The drug was given orally in doses of 75 to 300 mg. a day for periods of up to three months. The total effects are, however, less than those of sympathectomy and some patients experience no benefit.

Edwards *et al.* (1952), Droller (1953), and Betts (1954) have reported favourable results from the intra-arterial injection of tolazoline in cases of senile arterial obstruction. After a test dose of 25 mg., further doses of from 50 to

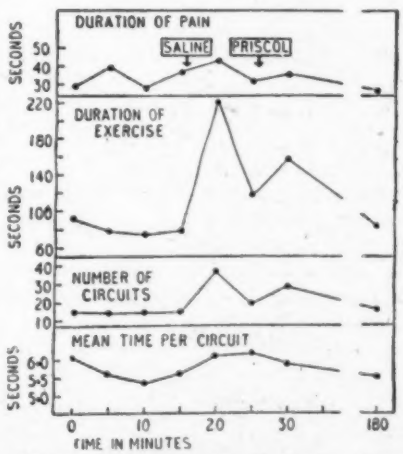

FIG. 2.—The effect of an intravenous injection of normal saline and of 10 mg. of tolazoline ("priscol") in a patient suffering from intermittent claudication. Exercise tolerance, as reflected by the amount and duration of exercise, was increased to a greater extent by saline than by tolazoline (reproduced, by permission, from the *Quarterly Journal of Medicine*, 1952, **21**, 169).

100 mg. may be given at weekly intervals. The treatment may produce objective improvement in ischaemic necrosis and symptomatic benefit in patients with persistent cold feet, but has no effect on intermittent claudication.

Many patients with symptoms primarily referable to the skin will improve after sympathectomy, but the selection of suitable cases in the elderly grows more difficult with increasing age.

Symptomatic Relief

Elderly patients often sleep badly and are especially liable to be kept awake by the discomfort which arises from cold feet and cramps. They are often helped by a regular dose of a barbiturate, but it should be remembered that old people often react unusually to these drugs and may become dizzy and disoriented. Simpson (1954) finds methylpentynol (" oblivon," " somnesin ") in doses of 1 g. a safe and useful hypnotic in the elderly.

There is a further group of patients who develop a painful redness of the feet of the type described by Lewis (1946) as erythralgia. These are best advised to avoid dependency of the limb and to sleep with the feet outside the bedclothes, as the burning sensation is worse when the feet are warm. Sympathectomy should be considered in this type of case. Some patients develop so-called rest pain, which resembles intermittent claudication although it occurs at rest. This usually demands the administration of analgesic drugs, and they are almost always necessary in cases with established gangrene. It is wise to begin with the simple analgesics such as aspirin and phenacetin before resorting to methadone (" physeptone ") or methorphinan (" dromoran "). The morphine group of alkaloids, which cloud consciousness to a greater extent, are best held in reserve. Chlorpromazine (" largactil "), which has a calming effect and tends to distract attention from pain, may prove valuable, especially in disorientated patients.

Treatment of Gangrene

Areas of threatened gangrene should be treated by the methods already described which improve the circulation to the skin. Once necrotic areas have developed, antibiotics should be administered and the areas kept clean and dry and exposed to the air. Pain is usually severe and demands the administration of analgesics. Local application of heat must be avoided. The decision when and where to amputate is best made in consultation with a surgeon. Occasionally occlusion of a main artery leads to a red and tender foot, but usually to massive gangrene, and high amputation is necessary. Diabetics form a special group. As we have seen, the typical lesion is in the smaller vessels and relatively conservative measures are desirable. Walker (1953) has reported good results in diabetic pre-gangrene and gangrene treated with oxytetracycline (" terramycin ").

Venous Thrombosis

The elderly are more prone to venous thrombosis than are the young. They frequently have a general slowing of the circulation to the legs and they are more often confined to bed either permanently from general weakness, arthritis, or hemiplegia, or temporarily from conditions such as acute respiratory infections and bouts of heart failure. To diminish this liability to venous thrombosis, the elderly should be confined to bed for as short a time as possible, especially after operations or acute infections. If this is impossible, passive or preferably active exercises of the legs should be instituted, and any complaint of pain in the legs or an unexplained rise of temperature should be immediately investigated with the possibility of venous thrombosis in mind. In established cases the advantages and disadvantages of anticoagulant therapy in the elderly should be carefully weighed. If the patient is in hospital it will usually be considered advisable. Measures such as paravertebral block or ligation of the femoral vein may be advised by a surgeon.

Conclusion

Peripheral vascular disease in the elderly presents special problems. The very fact of survival to old age suggests an arterial system relatively free from degenerative processes. Where symptoms occur the progress of the disease is relatively slow. The obese should be put on a low-fat diet. Diabetes is a common predisposing condition and if present should be treated. Little can be done to help patients with intermittent claudication. Prophylaxis against gangrene is, however, possible and important. It is always wise to give advice to a younger relative as well as to the patient, because the memory for recent events in the elderly is usually poor. When gangrene has developed, pain is severe and badly tolerated, and if amputation is withheld analgesics should be given freely. Diabetic gangrene can usually be treated conservatively with rest and antibiotics. Consultation with a surgical colleague is always advisable.

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ANTICOAGULANTS IN CORONARY DISEASE*

BY

A. RAE GILCHRIST, M.D., F.R.C.P., F.R.C.P.Ed.

AND

JOHN A. TULLOCH, *M.C.*, M.D., M.R.C.P.Ed.

(From the Department of Cardiology, Royal Infirmary, Edinburgh)

Before reviewing the use of anticoagulants in obliterative coronary disease, it is desirable first to consider briefly the pathological processes which result in myocardial infarction. Irregular thickening at the expense of the arterial lumen, and rigidity and tortuosity of the arteries, are the outward features of advancing atherosclerosis. Constriction of the channel, leading to a reduction in coronary blood flow, particularly if gradual and progressive, has important consequences. The most remarkable of these is the development of a collateral interarterial circulation, on which the future integrity of the muscle cells depends. As its coronaries become sclerotic the heart strikes a balance between the rate of narrowing and the development of anastomoses. Tissue anoxia appears to be the main stimulus for the development of interarterial anastomoses.

Infarct Formation

It is unfortunate that in clinical work the terms " coronary occlusion," " coronary thrombosis," and " myocardial infarction " continue to be used synonymously. They

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are in fact distinct pathological entities and can occur independently (Ravin and Geever, 1946). Coronary atherosclerosis is their common denominator. For the classical clinical syndrome characterized by the acute onset of precordial pain of anginal type, with a greater or less degree of shock and followed by the early development of a variety of signs of tissue destruction, the term "acute myocardial infarction" should be reserved. This is the state of affairs in which as a general rule an infarct can be diagnosed with confidence, located with accuracy electrocardiographically, and treated effectively with anticoagulants.

The term "coronary occlusion" should be reserved for an obliteration of the arterial lumen at a site determined by a local advance in the atherosclerotic process in the intima of the artery. Sclerotic occlusions can apparently occur independently of acute thrombus formation. It is a more gradual process and does not necessarily result in the formation of a circumscribed infarct, even when a relatively large artery is blocked—a fact which illustrates the importance of an adequate collateral circulation through the myocardium. In a pathological sense coronary occlusions—and they are not infrequently multiple—are the usual basis of the production of angina pectoris (Blumgart *et al.*, 1941).

Thrombosis of a coronary artery or a large branch is a common but not an invariable cause of an acute myocardial infarct. Tissue necrosis is the immediate result of acute and sustained ischaemia. Nevertheless, injection studies of the coronary circulation supplemented by careful dissections indicate that, if the obliterative arterial disease develops slowly enough, anastomotic channels gradually increase in number and may ultimately yield a supply of blood at sufficient pressure to provide a reasonably efficient reserve. In these circumstances an area of myocardium, which would otherwise perish, can survive despite acute thrombus formation. On the other hand, if a major artery is suddenly blocked by a local thrombus and the remainder of the coronary tree is comparatively healthy, or if for some unknown reason anastomoses have failed to develop, then a circumscribed infarct is the inevitable result (Ravin and Geever, 1946).

An infarct may form in the absence of a coronary thrombosis. Extreme narrowing of the arteries, a grossly inadequate collateral circulation, and excessive demands on the part of the myocardium may result in such an acute degree of coronary insufficiency that local ischaemia leads to asphyxial necrosis and even to infarct formation. It must then be assumed either that the amount of cardiac work performed was extreme and in response to some exceptionally severe and sustained demand, or that the local coronary supply was abruptly reduced to minimal amounts. Acute coronary insufficiency of this nature commonly results in a patchy subendocardial necrosis (Horn *et al.*, 1950). In these circumstances the clinical signs of tissue destruction are slight and transient.

Clinical Diagnosis of Infarction

It can therefore be understood how varied are the consequences of coronary disease, and how important is the balance struck between obliterative processes on the one hand and compensatory collateral channels on the other. Angina pectoris, acute coronary insufficiency, and acute myocardial infarction are overlapping syndromes, often difficult to distinguish clinically, yet commonly observed in greater or less degree in the one individual as fairly distinctive episodes in the life history of this form of advancing arterial disease. In general the recognition of frank infarct formation depends more on the metabolic derangements which accompany tissue necrosis than on the duration and severity of the pain, dyspnoea, or syncope which may mark the onset of the attack. Fever, leucocytosis, elevated sedimentation rate, increased serum fibrinogen, and augmented excretion of urinary urobilinogen (Evans *et al.*, 1952) are indications of the body's general reaction to myocardial necrosis. In these circumstances multiple lead electrocardiograms repeated over the course of a week or two almost invariably reveal the site and extent of the area infarcted and its rate of healing.

The Therapeutic Problem

These pathological and clinical concepts imply that the fundamental problem in treatment is the control of coronary atherosclerosis. The application of measures known to favour a regression of the intimal lesions or even procedures designed to prevent an advance in the obliterative process, together with the development of a reserve anastomotic circulation, would be major therapeutic achievements. Anticoagulants fall far short of these ideals.

Nevertheless, evidence is accumulating which indicates that an upset of the control of intravascular clotting commonly occurs after an acute myocardial infarction. It would be even more helpful to know if the increased coagulability of the blood observed in the early days of the illness (Ogura *et al.*, 1946) antedates the acute infarction. Unfortunately, techniques for the estimation of the clotting tendency of blood are open to wide individual variation and the evidence from different laboratories is conflicting. Beaumont *et al.* (1953) concluded that hypercoagulability persisted up to forty-eight hours after the infarct was sustained, to be succeeded by a reduced clotting tendency for approximately the next ten to fourteen days. Thereafter a variable degree of hypercoagulability was usually maintained for a few weeks. Further information on this aspect of coronary disease is highly desirable, particularly from the point of view of the prevention of infarction, notably when premonitory anginal symptoms give a clue to its early occurrence.

Myocardial infarction is a disease of extremes: the mildest examples may pass undetected, and the severest attacks are commonly immediately fatal. The overall mortality rate of first attacks is not known. For the large intermediate group of average or more than average severity, as encountered in hospital practice, the illness is commonly punctuated by complications which add greatly to the gravity of the situation. If not immediately fatal, they usually prolong convalescence and subsequently shorten the total survival period. The mortality rate for hospital patients suffering from acute infarction averages 33% in this country during the first six weeks, but it varies appreciably in different localities. For example, a consecutive series of patients observed in the Edinburgh Royal Infirmary, and known to have sustained transmural damage in an acute form, had a mortality rate of 41% (Tulloch and Gilchrist, 1950).

In the first six weeks the main and commonly fatal complications of acute infarction are shock of moderate to severe degree (29%), congestive heart failure (29%), and thrombo-embolic episodes (28%) (Gilchrist, 1952). There is no denying that in the early weeks the illness runs a treacherous and for the most part an unpredictable course. Even in the mildest cases a thrombo-embolic episode can cause disaster. One myocardial infarct may follow on another without the slightest warning, even within a few days of the original attack. Only in retrospect are there "good-risk" cases of acute myocardial infarction.

It is not yet known whether anticoagulants, restricted in use to the first four weeks, influence the ultimate prognosis, though the evidence indicates an increased survival rate for these first few weeks. By permitting a relatively larger number of individuals to survive the acute phase, some of whom might otherwise have been expected to die, it is possible that the group of patients receiving anticoagulants may experience in the year or two following the attack a higher mortality than the conservatively treated controls. We have as yet insufficient information to permit of firm conclusions on this aspect of anticoagulant treatment.

The ultimate prognosis is also far from satisfactory. Our hospital experience indicates that, for every 100 conservatively treated males, approximately 60 survive the first six weeks of the acute illness. At the end of one and a half

years from the onset half are dead. Of the original 100 only 40 survive the fourth anniversary of the acute attack. These findings paint perhaps too gloomy a picture, but they are an example of the course followed in a hospital series.

An analysis of the causes of death amongst the 60 conservatively treated males surviving the first six weeks of hospital treatment indicates that a recurrence of the myocardial infarct accounts for 14 of the 20 deaths observed in the four-year "follow-up," in addition to which nine patients had non-fatal recurrences. It is clear that having survived one myocardial infarct the hospital patient is more likely to die from a further attack than from any other cause, and commonly within a year. That there is an urgent need for the prevention of recurrences is now obvious, but as yet it is too early to assume that continued long-term anticoagulant therapy reduces the dangers. Detailed and well-controlled studies are fully justified and deserve to be continued.

Objects in Anticoagulant Therapy

The objects in using anticoagulants are worth re-emphasizing. In the presence of an acute infarct these drugs may be employed (1) to prevent any extension or propagation of the original thrombus, if one be present; (2) to prevent the formation of secondary thrombi, whether endocardial in site and underlying the infarct or in the peripheral veins of the leg or elsewhere—by this means the risk of the escape of clot into the general arterial or pulmonary circuits may be lessened and the frequency of frank embolic complications reduced; and (3) to promote the dissolution, absorption, or recanalization of the original or secondary thrombi—experimentally, as shown by Wright *et al.* (1952–3) and Jewell *et al.* (1954), there is much to support this contention.

If we apply these theoretical considerations to the clinical problems of coronary disease, it is reasonable to suppose that anticoagulants might prove helpful, not only in the treatment of acute infarction but in its prevention.

Response to Anticoagulants

The clinical history indicates that perhaps 30% of major cardiac infarcts are preceded by attacks of acute coronary insufficiency. Premonitory attacks of angina, often spontaneous, sometimes nocturnal, and commonly more severe and protracted than the usual effort pain, may recur in an irregular way over a period ranging from a few hours to a matter of a week or two before the major infarct is sustained. Under these difficult and treacherous conditions the encouraging results of Nichol *et al.* (1954) justify the prompt use of anticoagulants, with the hope of preventing the early development of acute myocardial damage. When unsuccessful, necropsy studies in these circumstances would be of particular value.

A claim can also be made for the long-term use of anticoagulants for the prevention of recurrences after one or more infarctions have been sustained. Careful and systematic supervision of comparative groups over a number of years is required before reliable conclusions can be drawn regarding the value of anticoagulants under these conditions. Our experience to date is encouraging, but it yet remains to be determined whether the long-continued use of an anticoagulant justifies the troubles and risks involved in this form of treatment (Nichol and Borg, 1950).

It must be appreciated that anticoagulant therapy is only one aspect of the care of the patient stricken with an acute infarct. Other measures—for instance, the provision of adequate rest, the treatment of shock, and the prevention of congestive heart failure—are of equal if not greater importance.

So many factors influence the immediate prognosis in cardiac infarction that the results of treatment are difficult to assess. The age of the patient, the sex, the frequency of previous attacks, the severity and duration of the initial shock, the occurrence of congestive heart failure, and the promptness with which treatment is applied are among the important factors influencing the immediate outcome. Furthermore, in contrast to the assessment of many other remedies used solely for their curative properties, the appraisal of anticoagulants is rendered more difficult as reliance must be placed on their powers to prevent serious complications. No dramatic response follows their use, but their value is shown by a reduction in the anticipated death rate and by a diminution in the incidence of thrombotic complications.

In recent years confirmation of the earlier claims made for anticoagulants in acute infarction has come from many independent workers using adequate control groups. Some of these results are incorporated in Table I, from which

TABLE I.—*Results Obtained in Recent Years by Various Workers Using Simultaneous Control and Treated Groups*

Author	Anticoagulant Group			Control Group		
	Cases	Deaths	Mortality %	Cases	Deaths	Mortality %
Schilling (1950) ..	60	10	16·7	60	24	40·0
Tulloch and Gilchrist (1950) ..	70	16	22·8	84	34	40·5
Rashkoff *et al.* (1952)	142	18	12·7	145	38	26·2
Loudon *et al.* (1953) ..	75	19	25·3	125	51	40·8
Wright, Beck, and Marple (1954) ..	589	93	16·0	442	103	23·4
Total ..	936	156	16·6	856	250	29·2

The findings substantiate the earlier claims that anticoagulants are capable of halving the death rate in the first six weeks after acute myocardial infarction.

it is evident that in general the death rate over the first six weeks is halved amongst those receiving anticoagulant therapy.

Considering the relatively good prognosis of the mildest attacks of myocardial infarction, Russek and Zohman (1952) have doubted the necessity or desirability of using anticoagulants as a routine measure in all cases. However, the practical results obtained to date provide the best justification for using these drugs and far outweigh the theoretical criticisms and misapprehensions of Evans (1954).

Our experience with anticoagulants in the treatment of acute infarction now extends over the past seven years, and is summarized in Table II. Only the 1947–50 series of

TABLE II.—*Analysis of Our Seven-year Experience of the Anticoagulant Treatment of 321 Consecutive Hospital Patients Suffering from Acute Myocardial Infarction*

	Cases	Deaths	Mortality %	T.-E. Episodes	Incidence %
Dicoumarol series (Tulloch and Gilchrist, 1950) ..	70	16	22·9	9	12·9
Tromexan series (Tulloch and Gilchrist, 1951) ..	87	16	18·4	4	4·6
New series (1954):					
Tromexan	67	12	17·9	9	13·4
Dindevan	97	14	14·4	12	12·4
Total (1947–54) ..	321	58	18·1	34	10·6

The new series includes an additional 164 patients receiving either "tromexan" (ethyl biscoumacetate) or "dindevan" (phenylindanedione). The average mortality rate for the first six weeks is 18.1% and the average incidence of thrombo-embolic episodes is now 10.6%.

dicoumarol-treated patients was compared with a simultaneous control group. It was then shown that the difference in mortality and in thrombo-embolic episodes was statistically significant, the death rate being halved in the treated group and the thrombotic complications being reduced to an even greater extent. With the passage of time, as shown in Table II, the mortality rate has fallen from 22.9% in the original treated series to 14.4% in our most recent experience. This reduction is largely attributable to the inclusion in recent years of a greater proportion of less acutely ill patients and to a less extent to greater experience in the handling of these drugs. We do not claim that the 41% mortality rate of the 1950 control group applies to our current hospital practice. If past experience is a guide, a mortality rate of approximately 28% might be anticipated in an Edinburgh control group at the present time. Similarly, the statistical analysis displayed in Table II does not

warrant the claim that one anticoagulant is more or less efficient than another.

A consideration of the major causes of death in the first six weeks after an acute infarction has revealed that the overall reduction in mortality, observed when anticoagulants are in use, cannot be attributed solely to a decrease in frank thrombo-embolic deaths. It appears, for instance, that the early and efficient use of heparin followed by an oral anticoagulant may exert a favourable influence on the outcome of the shock syndrome (Gilchrist, 1952; Loudon *et al.*, 1953). In a general way it is often true that one complication is soon followed by another. If survived, the severer grades of protracted cardiogenic shock predispose to congestive failure. Both clinical and pathological observations (Jordan *et al.*, 1952) indicate that thrombo-embolic episodes are more common in those who develop these complications. It may be that by controlling the thrombotic tendency, early anticoagulant therapy may limit the size of the original infarct, save uninfarcted muscle, and thereby prevent an advance in the vicious circle of thrombosis, infarction, shock, and hypotension. Alternatively, it is possible that anticoagulants may exert effects other than those directly concerned with blood clotting, which may prove beneficial to these gravely ill patients. The available evidence clearly indicates that the prompt use of anticoagulants is to be encouraged if serious difficulties are to be avoided and the mortality rate reduced to a minimum.

Laboratory Control

No anticoagulant is uniformly successful, despite as strict dosage control as laboratory methods permit. Notwithstanding daily prothrombin times, suitably maintained in the so-called therapeutic range by appropriate adjustment of the oral dosage from day to day, a minority of patients will develop thrombo-embolic complications. It is probable that such episodes are more likely to occur if the use of heparin or other anticoagulant has been postponed even for 24 to 48 hours. The greater the interval elapsing between the production of the infarct and the development of a satisfactory control of the clotting tendency, the more probable is the formation of intraventricular clot and hence the subsequent detachment of emboli.

No anticoagulant is entirely free from the risks of haemorrhage, even despite strict laboratory supervision. Close watch must be kept for bleeding, the urinary tract being the most common source. We are fortunate in that the Edinburgh Royal Infirmary has a well-organized and efficient laboratory service. The daily dose is regulated according to the prothrombin time, and in actual practice serious haemorrhage is seldom encountered. Transfusion has been required on five occasions. Bleeding, perhaps no more than microscopic in amount, is encountered in 11% of patients, despite careful laboratory control and the exclusion of those patients known to suffer from anaemia, gross renal or hepatic disease, and ulceration of the gastro-intestinal tract. Advanced pregnancy, open wounds, raw surfaces, and recent surgical procedures indicate the exercise of great caution in the use of these drugs. If haemorrhage occurs, as it occasionally will in spite of every care, the anticoagulant in use should be withheld, vitamin K_1 prescribed, and if necessary a blood transfusion begun.

Of the various vitamin-K preparations carefully tested by Douglas and Brown (1952), including the water-soluble K analogue, only vitamin K_1 was found to be a reliable and efficient antidote capable of blocking completely the action of therapeutic doses of dicoumarol and ethyl biscoumacetate. By its use excessive hypoprothrombinaemia could be corrected within a few hours. Toohey (1954), recommending smaller doses (5–50 mg.) of vitamin K_1 than those commonly employed, emphasizes the need for caution when vitamin K_1 is administered in the presence of advanced hypoprothrombinaemia lest the risk of haemorrhage is replaced by the dangers of thrombosis. Prothrombin times repeated at intervals of a few hours can be of value in determining the necessity for further doses of the vitamin. If bleeding occurs, persists, and is profuse, there should be no hesitation in transfusing with fresh whole blood.

One consequence of undertaking the long-term treatment of a selected group of patients known to have sustained one or more myocardial infarcts is the recognition that the interval between successive prothrombin times may be lengthened with safety. As a general rule, after two to three weeks of daily blood samples it is justifiable to regulate the oral dosage by prothrombin estimations on alternate days. On beginning out-patient supervision the patient usually attends twice weekly for two to three weeks and, provided the oral dose is reasonably stable and the prothrombin times within the therapeutic range of two to two and a half times the control figure, once a week for the following two to three months. Later a blood sample once a fortnight may prove sufficient in the co-operative patient, who understands the significance of any unusual bleeding and who may be trusted with a supply of vitamin K_1 for emergency use. From experience of the management of 227 out-patients receiving anticoagulants for a variety of conditions, Tulloch and Wright (1954) concluded that with reliable laboratory facilities long-term treatment was relatively safe and fully justified.

Necropsy Findings

Support for the conclusions reached from clinical experience is also found in the analysis of the necropsy findings in 71 patients. Post-mortem examinations were made on 34 patients dying during the course of anticoagulant therapy, and on 37 patients from whom these drugs were withheld. Only a brief review of the major findings are mentioned here as more detailed studies are in progress.

The presence of recent acute infarction was demonstrated in all the cases. In the anticoagulant series ante-mortem mural thrombi were found in 13 instances (38%), as compared with 19 (51%) in the controls. In only 5 (14.7%) of the treated group were peripheral or pulmonary thrombotic lesions recognized, as compared with 15 (40.5%) in the control series. It is significant that thrombo-embolic lesions were therefore two and three-quarter times more common in the untreated than in the treated group. Many of these patients had multiple lesions involving the lungs, kidneys, or spleen, which had not been diagnosed clinically. The difference between the two groups is all the more striking when allowance is made for the fact that in our earlier experience the control of the prothrombin times was less intensive and less well maintained from day to day than is our current practice. Furthermore, the present analysis of thrombo-embolic lesions is confined to the pulmonary and general circulations without the inclusion of fresh cardiac damage in the form of reinfarction or extension of the original myocardial infarct responsible for the acute illness. Wright, Marple, and Beck (1954) noted that undiagnosed thrombo-embolic episodes were more frequently found at necropsy in the untreated than in the treated cases—a finding which emphasizes that comparison based on clinical studies underestimates the contrast between the two groups. Our pathological observations therefore support the contention of these authors that under the influence of anticoagulants the incidence of thrombo-embolic lesions is appreciably lessened.

Summary

The mechanism of the production of myocardial infarction is discussed in the light of newer knowledge concerning the arterial lesions of obliterative coronary disease on the one hand and the development of a subsidiary interarterial anastomotic circulation on the other.

In general the clinical recognition of frank infarct formation depends more on the metabolic upset which accompanies tissue destruction than on the duration of the pain, dyspnoea, or syncope, any one of which may mark the onset of the acute attack.

A disease of extremes, acute myocardial infarction runs a treacherous and unpredictable course. There are only "good-risk" cases in retrospect.

Evidence continues to accumulate in support of the contention that anticoagulant drugs used early and efficiently, and continued for a minimum of four weeks under strict laboratory control, are capable of halving the death rate and reducing the incidence of thrombo-embolic episodes commonly observed during the first six weeks of the illness.

Necropsy experience substantiates the claim that anticoagulant therapy reduces the frequency of thrombo-embolic lesions.

The overall reduction in mortality cannot be attributed solely to the decrease in frank thrombo-embolic deaths. It appears that the severer grades of cardiogenic shock are favourably influenced by these drugs.

A claim can also be made for the prompt use of anticoagulants when a succession of attacks of acute coronary insufficiency suggests that myocardial infarction is imminent. There is also a justification for their use in selected patients on a long-term basis in the hope of preventing recurrences amongst those who have already sustained one or more myocardial infarcts.

No anticoagulant is uniformly successful. None is devoid of risk. Their successful use demands close clinical supervision supplemented by reliable laboratory facilities. Efficiently used, anticoagulants make a distinct contribution to the treatment of acute myocardial infarction.

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Scientific Research in British Universities 1953–54 (H.M.S.O., price 10s. net) is a massive 500-page paper-backed book issued by the Department for Scientific and Industrial Research in agreement with the Agricultural and the Medical Research Councils. The information in it has been collected direct from the heads of University Departments by the British Council. The Universities are taken alphabetically, and each department is listed, with the names of the head of the department and the permanent staff and a broad description of the research in progress during 1953–4. Under London University, the medical schools and institutes of the Postgraduate Medical Federation are separately scheduled. There is an index to the names of all research workers mentioned, and for the first time a detailed subject index.

DISTRIBUTION OF MICROFILARIAE OF O. VOLVULUS IN THE SKIN

ITS RELATION TO THE SKIN CHANGES AND TO EYE LESIONS AND BLINDNESS

BY

W. E. KERSHAW, V.R.D., M.D., D.T.M.&H.
Lecturer in Medical Parasitology, Liverpool School of Tropical Medicine

B. O. L. DUKE, M.B., D.T.M.&H.
Pathologist in Charge, Helminthiasis Research Scheme, Kumba

AND

F. H. BUDDEN, M.B., D.O., D.T.M.&H.
Colonial Medical Service

In the course of experiments undertaken in 1953 to investigate the quantitative aspects of the transference of *Onchocerca volvulus* from man to the vector, *Simulium damnosum*, in the British Cameroons, it became necessary to estimate the number of microfilariae in the skin which might be available for ingestion by the fly when taking up its blood meal. Skin snips taken from different parts of the body were weighed on a torsion balance, teased in saline on a slide, and the number of microfilariae issuing forth in a wet film were then counted. The results obtained in the British Cameroons had far-reaching implications concerning the clinical and epidemiological aspects of the infection, and, consequently, similar investigations were carried out in conjunction with ophthalmological studies in areas of Northern Nigeria where blindness is common. In 1954 these combined investigations were repeated in the British Cameroons.

Little attention seems to have been paid to the number of microfilariae to be found in a sample of skin, except that it seems to have been generally assumed that the number could be taken as a very rough measure of the intensity of the infection. The prevalent impression seems to have been that the microfilariae were of very uneven distribution, and that the number in adjacent portions of skin was extremely variable.

Buckley (1949), whilst in East Africa, made a quantitative study by counting the number of microfilariae issuing from skin snips which appeared on inspection to be of about the same size. The snips were taken from many corresponding sites on both sides of the trunk and limbs of a native of Kenya. Buckley concluded that the distribution was very uneven, was without pattern, and that because of the discrepancies the method he described could not be relied upon for a quantitative estimate of the degree of infection.

Blacklock (1926) and Mazzotti (1951) investigated the distribution in a qualitative manner by recording whether skin snips taken from different sites in different individuals were positive or negative. In Sierra Leone, Blacklock found microfilariae most commonly in the loins, next in the thighs, then in the scapular region, and rarely in the ankles. In Mexico, Mazzotti found them irregularly in the entire skin in the upper half of the body and pelvic girdle and rarely in the skin of the lower extremities.

Material and Methods

Samples of the skin were removed by inserting (almost horizontally) in the skin a very fine entomological pin

mounted in a needle holder; the point was then raised, lifting a cone of skin about 2 mm. in height and diameter. This cone was removed with a new safety-razor blade, so that a piece of dermis about 2–3 mm. in diameter was removed with a slightly larger circle of epidermis. No blood was present on the snip, though the vessels in the bed from which it had been removed later oozed very slowly.

The piece of skin was then weighed on a torsion balance, made by the White Electrical Instrument Company, Ltd., London, and designed to weigh up to 10 mg. with an accuracy of 0.02 mg. With this balance, weighing was completed in perhaps a quarter of a minute. The snip was then teased out with stout needles, in about 30 c.mm. of saline on a slide, and examined unstained without a coverslip for motile microfilariae which emerged from the fragments. It was our practice to tease for about one minute, then to count the microfilariae. An equal volume of human serum was added, and, after drying, this film was fixed in methyl alcohol and stained with hot Mayer's haemalum for later examination. A thick blood film was made from 50 c.mm. of blood obtained by finger-prick, dehaemoglobinized, and fixed and stained in a similar manner.

In the British Cameroons snips were taken from the skin over the ankles, calves, thighs, the deltoid region, the forearms and hands, and from the trunk, and often from the buttocks, from the skin at the outer canthus of the eye, and from the conjunctiva. Later, when the pattern of the distribution had become clear, the snips were limited to the calf, buttocks, deltoid region, outer canthus of the eye, and the conjunctiva of one side, unless some special feature suggested further examination.

Over 200 cases were examined by multiple skin snips.

Results

It is convenient to present the results in such a manner as to illustrate the relation of the distribution of the microfilariae to local anatomical factors, then the relation of the general pattern to the skin changes, and, finally, the relation to eye changes and to blindness.

Local Factors Influencing Distribution

1. *Concentration of Microfilariae in Neighbouring Areas of Skin.*—In order to determine whether the distribution of the microfilariae was as uneven as has been supposed, separate but contiguous skin snips were taken from an area 1 cm. square on the shoulder, on the thigh, and on the calf of a man with a heavy infection. Care was taken that the snips in the groups taken from each region were as nearly as possible of the same size, so as to ensure that about the same area and depth of skin was removed in each snip. In the group taken from the left thigh two additional snips, one larger and the other much smaller, were taken. The results given in Table I show that the concentration of microfilariae is uniform in an area of the skin 1 cm. square, and that within the limits of the size of the skin snips taken, limits within which a reasonable skin snip is likely to fall, the weight of the snip, and therefore its thickness and area, does not influence the result.

TABLE I.—*Showing the Number of Microfilariae of O. volvulus Found in a Wet Film Made From Weighed Separate but Nearly Contiguous Skin Snips Taken From Within an Area 1 cm. square From the Skin Over the Left Deltoid Region, the Left Thigh, and the Left Calf*

Region	Weight of Skin Snips (mg.)	No. of mf. in Wet Film	No. of mf. per mg. of Skin
Left deltoid	1·47	5	3·4
	1·53	6	3·9
	1·74	12	6·9
	1·15	5	4·4
			Mean 4·7±1·5
Left thigh	2·75	92	33
	2·24	55	25
	2·63	76	29
	2·12	75	35
	0·46	16	35
	4·60	164	35
			Mean 32±4
Left calf	1·22	268	220
	1·23	228	185
	1·10	241	220
	0·60	115	192
			Mean 204±18

2. *Concentration of Microfilariae in the Different Types of Local Skin Lesions.*—The relationship of the concentration of the microfilariae and the different types of skin lesions is considered when the general pattern of the developing infection is discussed, but it is convenient here to state that we found the concentration to be very closely related to the condition of the skin at the point at which the snip was taken. Skin snips taken from areas of skin showing no obvious abnormality were found to contain few or no microfilariae. On the other hand, skin snips taken from areas which had undergone the change of lichenification contained a number of microfilariae which was roughly proportional to the intensity of the change. When skin snips were taken from advanced cases of onchocerciasis from areas in which the appearance of the skin resembled that presented by tissue paper which has been crushed and then flattened the concentration fell. Fibrous scarring, particularly when followed by leucoderma, is accompanied by a pronounced fall in the concentration. Keloid scarring also contains lower concentrations than the surrounding skin.

3. *Concentration of Microfilariae on the Dorsal and Ventral Aspects of the Trunk and the Extensor and Flexor Aspects of the Limbs, and its Relation to the Skin Lesions.*—Since the skin changes occur earlier and become more severe on the extensor aspects of the limbs and on the dorsal aspects of the trunk, and since the concentration of microfilariae was found to be closely related to the condition of the skin sampled, the pattern of the distribution of the microfilariae and the skin lesions was investigated in two cases in detail. Skin snips were taken in pairs from many corresponding sites on the trunk and limbs, one snip of each pair being from the ventral or flexor aspect of the trunk or limb, the other being taken from the dorsal or extensor aspect. Similar results were obtained in both cases: these showed clearly that the concentration of microfilariae and the lichenification of the skin are more pronounced on the dorsal aspect of the trunk and the extensor surface of the limbs than on the ventral aspect and the flexor surface.

4. *Concentration of Microfilariae in the Skin in Relation to the Nodule.*—(*a*) *The immediate vicinity of the nodule*:—It has been generally believed that the microfilariae were more numerous in the immediate vicinity of the nodule, and in three cases snips were taken from the skin over the nodule and from sites near by. The results showed that the skin over the nodule contained fewer microfilariae than that about 10 cm. from the nodule. This finding is the converse of the usual belief, and the fall in the microfilarial concentration may be due to the local changes in the skin over the nodule consequent on stretching and atrophy. (*b*) *The same anatomical quarter as the nodule*:—Despite the finding of a higher concentration 10 cm. away from the nodule than over the nodule itself, it was evident from the examination of those with early or light infections that in those in which there was only one or two nodules, and in which the microfilarial concentration in the skin was low, the few microfilariae present might be found only in the same anatomical quarter as the nodule.

5. *Concentration of the Microfilariae in the Skin Compared with that in Deeper Tissues.*—One of the cases examined had an inguinal hernia which was operated upon by Dr. E. A. Fejer. The samples of tissues removed at operation were weighed and treated as skin snips. No microfilariae were found in the fibrous tissue of the hernial sac: the concentration was low in the capsule and pulp of an enlarged femoral gland at the site of operation which did not contain adult worms, and the wall of a nodule containing gravid worms removed from the iliac crest of the same side contained a concentration of the same order as in the near-by skin.

6. *Lack of Variations During the Day and Night and from Day to Day.*—Since *S. damnosum* bites only during the day,

it seemed advisable to see whether the microfilariae might show a corresponding periodicity similar to the correlation of the biting habits of *Chrysops silacea* and the daily periodicity of *Loa loa*. Two cases of infection were examined by day and by night and several were examined on more than one day. No marked changes in the concentration of microfilariae were found. It is clear that the concentration of microfilariae does not differ greatly during the night and day or from day to day.

Relation to Skin Lesions

A relation between the general pattern of the distribution of the microfilariae in the skin and the development of the skin changes was found in each individual examined, with perhaps such minor modifications as have been described, and this relation was general throughout the particular community exposed to infection.

In an early or lightly infected case the microfilariae may be found only in small numbers in the same anatomical quarter as the nodule.

In a case of moderate intensity the microfilariae are most numerous in the ankles, calves, and buttocks, then in the thighs and the waist, and are usually few or are absent in the shoulders, arms, and face. Though the nodules are most commonly found near the pelvis, this distribution of the microfilariae in such cases of moderate intensity seems to be largely independent of the exact position of the nodules. In some cases, however, there may be a local increase in the same anatomical quarter as the nodule compared with the corresponding quarter on the other side of the body. The concentration of microfilariae is proportional to the degree of lichenification, and is higher on the dorsal and extensor surfaces of the trunk and limbs than on the ventral and flexor surfaces.

As the case becomes more advanced, the skin of the ankles becomes fibrosed and the concentration of microfilariae falls. An example is shown in Table II. Later, the calves become fibrosed and smooth, with an extension of the local fall in the concentration.

In the "burnt out" case the microfilariae may be few, though the residual skin changes may be extreme. When the skin is severely affected by fibrosis, atrophy, scarring, or leucoderma, or when the condition described as "crushed tissue paper" or "lizard skin" occurs, few microfilariae are found.

TABLE II.—*Showing the Concentration of Microfilariae of O. volvulus in Skin Snips From an Advanced Case of Infection With Marked Skin Changes and Fibrosis over the Ankles. (Nodules Left Side of Chest, Outer Surface of Both Thighs, Both Iliac Crests, and the Right Trochanter)*

Site on Right Side	No. of mf. per mg. of Skin	Site on Left Side	No. of mf. per mg. of Skin
		Conjunctiva	0
		Outer canthus	0
Deltoid	8·1	Deltoid	1·1
Forearm	1·0	Forearm	1·5
Hand	0	Hand	1·8
Costal margin ..	3·8	Erector spinae	31
Buttock	71	Buttock	38
Thigh	95	Thigh	74
Calf	82	Calf	66
Ankle	0·6	Ankle	1·7

In general the number of palpable nodules increases throughout the progress of the infection.

Relation to Eye Lesions and Blindness

This was investigated in 1953 at Dadin Kawa and Gbulki in Northern Nigeria, and in 1954 at Bonjongo and Bimbia in the British Cameroons.

Anterior Segment Lesions.—At Gbulki, infected patients were classified in four groups according to the severity of the onchocercal keratitis and iridocyclitis—that is, those with: (1) no eye lesions, (2) early lesions of the anterior segment, (3) advanced lesions of the anterior segment, and (4) advanced lesions of the anterior segment in persons with "burnt out" skin lesions. In groups 1, 2, and 3 we found a progressive rise in the concentration of microfilariae in the legs and lower trunk associated with a spread of microfilariae to the shoulders, face, conjunctiva, and anterior chamber of the eye. This rise in concentration of microfilariae is followed by a fall in persons with "burnt out" skin lesions (group 4). The skin changes bore a similar relation, and there was a progressive rise in the number of nodules and in the average age of the four groups, reflecting the duration of their exposure to infection. The relation of the distribution and concentration of microfilariae to the skin lesions and to the changes in the anterior segment of the eye are shown in Fig. 1.

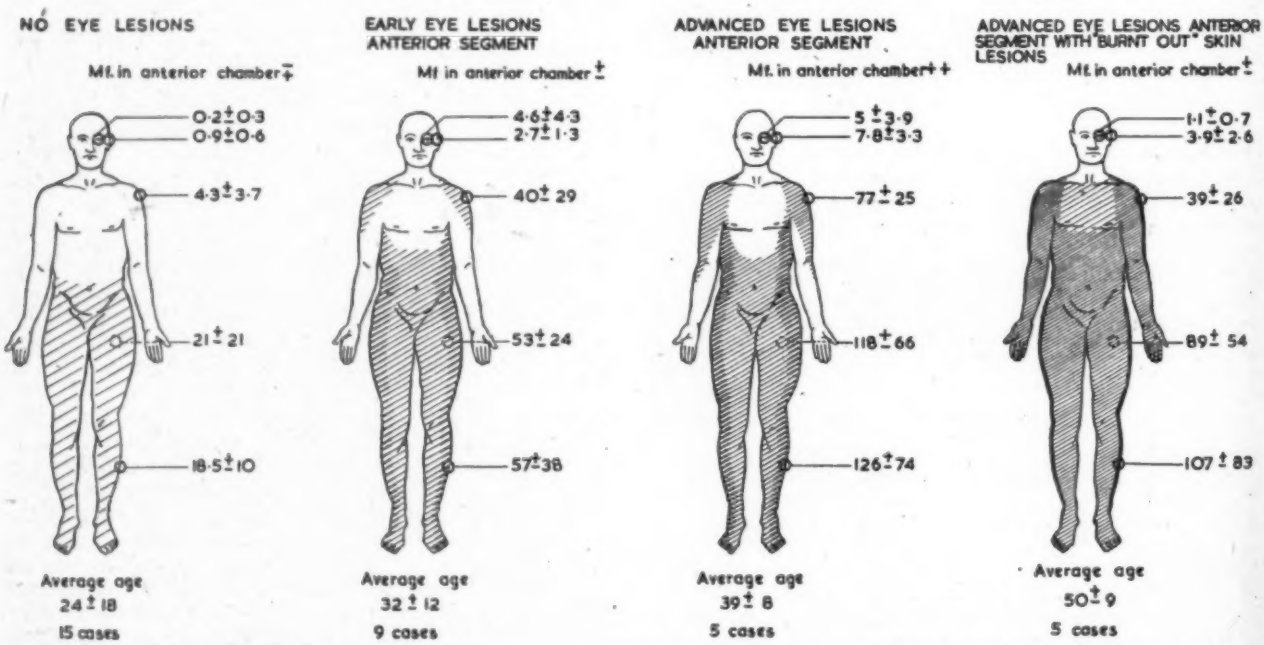

FIG. 1.—Showing the relation of the distribution and concentration of the microfilariae of *O. volvulus* to the skin lesions and to the changes in the anterior segment of the eye in the inhabitants of the village of Gbulki. The concentration is given as the number of microfilariae per mg. of skin over the calf, buttock, deltoid region, and the outer canthus of the eye, and of the conjunctiva. The areas with marked skin changes are shaded. The mean number of nodules found in the individuals in the four groups is 1·9±1·3, 4·2±3·2, 5·4±2·7, and 4·4±2·3.

The incidence of onchocercal eye lesions at Gbulki is so high that we were unable to collect a series of patients to serve as controls in the older age groups. At Bonjongo, however, eye lesions were less common and usually less severe. We were therefore able to collect a series of patients and to compare the distribution of microfilariae in those with anterior segment lesions and those with no eye lesions in the same age groups. These findings were analysed in two age groups, and Fig. 2 records the findings in those aged

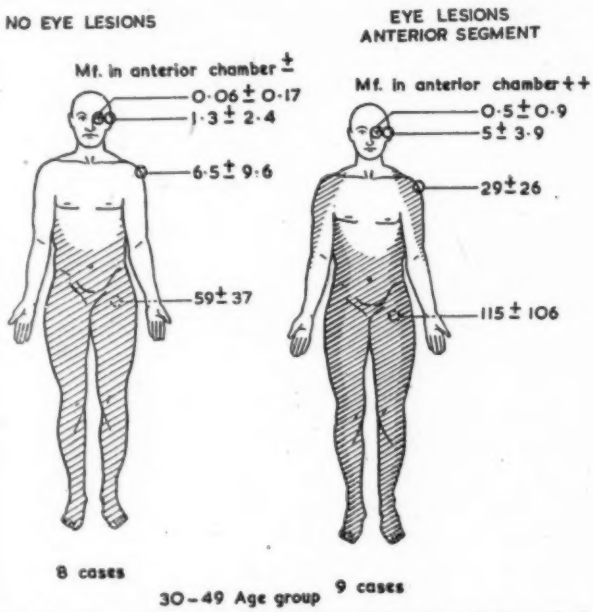

FIG. 2.—Comparing the distribution and concentration of the microfilariae of *O. volvulus* in those with no lesions of the eye and in those with lesions of the anterior segment in the age group 30–49 of the inhabitants of the village of Bonjongo. The concentration is given as the number of microfilariae per mg. of skin over the buttock, deltoid, and the outer canthus of the eye, and of the conjunctiva. The areas with marked skin changes are shaded. The mean number of nodules found in the individuals in this group is 4.6 ± 2.1 and 9.3 ± 4.9.

30–49. Similar results were obtained in those over 50. In both age groups the intensity of infection is higher and the spread of microfilariae more advanced in those with anterior segment lesions than in those whose eyes are not involved, showing that the resulting intensity of infection and not merely age and duration of exposure is the causal factor.

Posterior Segment Lesions.—The possibility of a corresponding relationship existing between the posterior segment lesions and the distribution and concentration of microfilariae is more difficult to assess because some anterior segment changes prevent examination of the fundus. At the places we visited no conclusive association between the development of posterior segment lesions and the spread of microfilariae to the head region could be demonstrated. Further evidence to which we refer in the discussion suggests that the pathogenesis of anterior and posterior segment lesions may be different.

Discussion

It is convenient to consider these findings first in their bearing on the mechanisms controlling the distribution of the microfilariae in the skin, on the transmission of the infection by the vector, and on the population dynamics of the parasite in the human host; secondly, to consider the relation of the distribution and the concentration of the microfilariae to blindness; and, thirdly, to discuss the significance of this definitive host–parasite relationship in the possible control of the infection, the prevention of blindness, and the treatment of infected individuals.

Much of this discussion must be speculative, but, since some of the apparently anomalous features of the infection are more easily understood when considered as part of a definitive host–parasite relationship involving the intensity of the infection in the individual and in the community, it is profitable to discuss the implications in some detail.

Population Dynamics of the Microfilariae

Before discussing the factors which influence the distribution of the microfilariae it is perhaps advisable to consider what little we know of the life history of the microfilariae of *O. volvulus*. We have no direct evidence of the longevity of the microfilariae, but from such information as is available on the results of treatment with suramin, in which it is assumed that the effect of the drug is wholly on the adult worm, and by analogy (with due caution) with other filarial infections in man, it appears that the individual microfilariae probably live for weeks or months. This belief, however, does not help us to determine whether the pattern and concentration of the microfilariae described as a result of our investigations have been built up by the slow accumulation of long-lived microfilariae over a period of years or whether the microfilariae are constantly being replaced with a relatively rapid population turnover. We are thus unable to say, in the case of an individual with an infection established at a particular level of intensity and harbouring an unknown number of functioning adult worms, whether the microfilarial distribution and intensity represents a balance between microfilarial destruction and replacement, or whether the concentration will continue to build up slowly without any effective suppressive mechanism.

We do not know whether the microfilariae lying in the tissue spaces of the superficial layers of the dermis remain static or whether they move rapidly from place to place within the skin. They are seen alive only in the aqueous humour in the anterior chamber of the eye, or in the saline surrounding the tissue in a skin snip, neither of which can be regarded as their normal environment. This problem is unlikely to be solved except by the observation of the microfilariae by direct microscopy of living skin.

Pattern of Distribution of Microfilariae in the Skin

It seems reasonable that in a light infection microfilariae should be found in a higher concentration in the same anatomical quarter as the nodule. That the microfilariae are fewer in the skin over the nodule is perhaps explained by morphological changes in the overlying skin due to stretching or to mild trauma.

The high concentration of microfilariae in the lower part of the leg and in the trunk in an infection of moderate intensity is perplexing, for, though the nodules are predominantly on the legs and pelvis, yet this high concentration in the lower extremities occurs irrespective of the position of the nodules. We think that a simple explanation depending upon a physical agency like gravity or some peculiarity of the superficial layers of the dermis in the legs is too specious, and any explanation must embrace not only the distribution as we have found it in West Africa, but also such results as may be found in the Central American form of the infection. Mazzotti (1951), working in Mexico, showed by qualitative examinations that more skin snips were positive in the upper portions of the body than in the lower; Blacklock (1926) had shown previously in Sierra Leone that more skin snips were found to be positive in the lower portion of the body than in the upper. If any inference can be drawn from their results and from ours in Nigeria, then we suspect that if the concentration of microfilariae in Central America were investigated by means of weighed skin snips it might be found to be higher in the upper part of the body than in the lower. Information on this point would enable us to be more definite about many of the underlying principles of the definitive host–parasite relationship.

We know nothing of the early life history of the adult worms, except for an occasional record of their having been found accidentally at operations, lying free in the tissues, usually in the inguinal region. The infective form is deposited by *S. damnosum* (the chief vector in West and

Central Africa) during biting, which occurs predominantly on the ankles and the lower parts of the legs. The developing and adult worms then presumably wander in the tissues much as does the adult *Loa loa*. Their progress is, however, not accompanied by Calabar swellings, and in consequence we do not know how widely they may migrate before becoming encapsulated, but there is no record of an adult *O. volvulus* crossing the eye. While those worms which are found in nodules are adult, it does not follow that encapsulation may not occur until some time after the migrating adult female has copulated and has begun to liberate microfilariae. If the rate of migration of the developing and adult worm were slow, and in consequence it remained in the region in which it was deposited as an infective larva by the vector, or if encapsulation were delayed, then the few adults found in a palpable nodule might be the only detectable representatives of a potentially larger population of worms producing microfilariae but moving slowly in the legs or encapsulated in deeper nodules. In this connexion it is interesting to note that *S. ochraceum*, a vector of onchocerciasis in Mexico, bites predominantly on the head and neck, the sites where the nodules are most commonly found in that area.

We are at a loss to explain why the concentration of the microfilariae should be higher and the skin lesions should be more clearly marked on the dorsal and the extensor surfaces of the trunk and limbs than on the ventral or flexor surfaces. It may depend upon differences in the detailed architecture of the skin in these situations, involving perhaps the vascular supply or the structure of the tissue spaces; similarly, an explanation is lacking for the localized distribution of psoriasis, lichen planus, and other skin conditions. On general grounds it seems unlikely that the microfilariae are attracted to the lesions, and it is more reasonable to assume that the presence of the microfilariae in the skin leads to the production of the lesions.

Relation of Distribution of Microfilariae to Transmission

In an established case of infection in West Africa the highest concentration of the microfilariae is in the legs, particularly in the calves and ankles, the area in which *S. damnosum* bites preferentially. The established case without atrophic skin lesions and the habits of the vector thus combine to facilitate the transfer of the parasite. This mechanism may be regarded as corresponding in space to the periodicity in time manifested by *Loa loa* and *Wuchereria bancrofti* with their appropriate vectors. As the case progresses and the skin changes of atrophy or fibrosis develop, accompanied by a fall in the concentration of microfilariae, this mechanism changes from one of enhancement of transmission to one of suppression.

Relation to Eye Lesions and Blindness

The occurrence of anterior-segment lesions is related to the presence of microfilariae in the anterior chamber and the head region consequent upon a spread of microfilariae from the lower parts of the body. This spread is associated with a high intensity of infection in the human host, and this in its turn probably reflects the duration and intensity of the exposure to which the host has been subjected throughout his life.

Figures being published separately by one of us (F. H. B.) show that where there is a high proportion of infected persons in a community infections are acquired early in life, their intensity rapidly rises, and a rise in the concentration of microfilariae in the head region often occurs. Blindness due to anterior-segment lesions, when expressed as a percentage of infected persons, is 23 times higher in these heavily infected communities than in lightly infected ones, and, furthermore, persons in the younger age groups are more often affected. By contrast, the incidence of blindness due to choroido-retinal lesions amongst infected persons is only six times higher in the heavily infected villages than in the villages where infection is light. These findings lend support to our suggestion that the anterior-segment lesions are closely related to an invasion of the anterior chamber by microfilariae. They also suggest that, although posterior-segment lesions are related to onchocercal infection, the mechanism of their production is different and possibly does not depend on the presence of microfilariae in the eye.

Possible Other Factors in Eye Changes

An understanding of the way in which the intensity of the infection affects eye lesions may well explain the apparent anomaly that onchocerciasis in West Africa is not uniformly associated with blindness. Other causes such as nutritional changes have been postulated in the past to explain such apparent anomalies. The occurrence of blindness in the inhabitants in some areas and not in others, the finding of eye changes in individuals in whom microfilariae were not found in the eye, and their absence in others in whom microfilariae were found thus require explanation.

We believe these anomalies can be explained by differences in the intensity of exposure of the community affecting the duration, intensity, and distribution of the infection in the individual.

Nutritional factors may, of course, as in malaria and sleeping sickness, affect the host–parasite relationship, but such a possibility must remain speculative until further knowledge is acquired.

Relation to Treatment and Control

We have little information at present on the manner in which the pattern of the distribution of microfilariae is altered by treatment with such drugs as the piperazines, which act on the microfilariae, or by suramin, which affects only the adult worm. But it is obviously of considerable importance to know whether after the use of diethylcarbamazine the infection regains its original intensity after a short or a long interval, an interval which will depend upon the natural population turnover of the microfilariae, appropriate to the stage and intensity of the infection at the time when treatment was instituted.

Our findings suggest that it may thus be practicable to ward off the eye changes in the individual by repeatedly reducing the microfilarial intensity at appropriate intervals by the use of this drug, or by interfering with the population turnover of microfilariae by killing the adults with suramin, or by a combination of both types of drug. Individuals exposed for many years to an intensity of transmission which could in this time produce eye changes may thus be protected even in the absence of control measures directed against the vector by limiting the established intensity of their infection below this critical level. Furthermore, an understanding of the method of the production of eye lesions has an immediate bearing on possible control measures directed against the fly, since repeated temporary reduction of the population of the vector, without attempting complete eradication, may possibly reduce the intensity of human infection below the level which is associated with eye changes and may maintain it below this level.

Summary

The concentration and distribution of the microfilariae of *Onchocerca volvulus* in the skin were estimated in people in the British Cameroons and in Northern Nigeria by counting the number issuing in a wet film made from skin snips weighed on a torsion balance and taken from different parts of the body.

The numerical distribution of the microfilariae was found to have a clear pattern, which in the Cameroons and in Northern Nigeria was related to the distribution and severity of the skin lesions and to eye changes and blindness.

Possible reasons for this distribution are discussed, and, from the relation to eye changes, conclusions are drawn concerning the possibility of the effective control of the infection and the prevention of blindness.

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INTRAMUSCULAR BENZATHENE PENICILLIN IN THE PROPHYLAXIS OF STREPTOCOCCAL INFECTION IN RHEUMATIC CHILDREN

BY

C. B. PERRY, M.D., F.R.C.P.
Professor of Medicine

AND

W. A. GILLESPIE, M.D., M.R.C.P.I., D.P.H.
Pathologist

University of Bristol and United Bristol Hospitals

In 1951 Szabo, Edwards, and Bruce described the preparation and chemical properties of a new penicillin compound—N,N'-dibenzylethylenediamine penicillin G (benzathene penicillin). Elias, Price, and Merrion (1951) showed that this substance marked a valuable advance in depot penicillin therapy, and that useful blood levels were maintained for as long as 144 hours after a single dose of 300,000 units, and for 12 days after 2.5 mega units. O'Brien and Smith (1952) reported that two injections at weekly intervals, or even a single injection of 2.3–2.5 mega units, gave excellent results in the treatment of gonorrhoea, 97% of the cases so treated being apparently cured. Further, fourteen days after the single dose appreciable blood levels of penicillin were found. Such a preparation clearly promised to be of value in the prophylaxis of streptococcal infection in patients who had suffered from rheumatic fever, and Stollerman and Rusoff (1952) reported the results of its use in 135 children. They found that 300,000 units maintained adequate blood levels for at least a week, 600,000 units for two weeks, and 1.2 mega units in most cases for four weeks. No patient developed a sore throat during treatment, but there were instances of temporary "bacteriological relapse" but with no evidence of clinical illness. These claims are so important that it appeared desirable to confirm them.

For this purpose a study has been made of children recovering from acute rheumatism or chorea in a hospital school.

Methods

Throat swabs were plated, within three hours of taking, on 5% horse-blood digest agar containing 1:700,000 crystal violet and incubated overnight in an anaerobic jar at 37° C. One colony from every plate with β-haemolytic streptococci was subcultured on blood agar and was grouped by the method of Maxted (1948). All group A cultures were tested for penicillin sensitivity by a ditch-plate method and sent for typing to the Streptococcal Reference Laboratory, Colindale. Serum penicillin levels were measured by the *Sarcina lutea* plate method (Welch, 1948) modified by diluting the suspension of the organism so that its final concentration in the plates was 1 in 2,000 of the original culture.

The study lasted from March 1, 1953, to February 28, 1954. During this period 53 rheumatic fever convalescent children were admitted and 48 were discharged. Their ages were from 6 to 16 years. The duration of their stay in hospital ranged from 83 to 316 days. The children were accommodated in two wards, where there were also some children with orthopaedic complaints. The number of rheumatic children in the wards at a time varied from 10 to 23, and the number of orthopaedic patients varied from 33 to 35 at any one time. Except for benzathene penicillin, no specific treatment was given during the study. Throat swabs were taken at weekly intervals from all the rheumatic patients, and from time to time from the orthopaedic patients. All group A streptococci were typed. From the results of the swabs, estimates were made, as described below, of the load of infection in the community—that is, the numbers who were carrying group A streptococci—and of the numbers of new infections which took place among the rheumatic children. Haemolytic streptococci of groups other than A were isolated occasionally, but were not considered further.

Twenty-two rheumatic children were given the specific treatment which was used for the first time on July 1. At first cases were chosen because they were persistent carriers of group A streptococci; later alternate admissions were treated. Fifteen of the treated children had been persistent carriers for from four to nine weeks before their first injection. The other seven had negative swabs for from two to seventeen weeks before the first injection. The treated children were distributed at random in the two wards. No child was treated until it had been in hospital for at least three weeks. Benzathene penicillin was given intramuscularly, into the buttock, in doses of 1.5 mega units contained in 5 ml. One child received five doses, seven children received four doses, six received three, five received two, and three received only one dose.

Serum penicillin levels were measured 4, 11, 18, and 25 days after the injection. The results are summarized in Table I. Most of the assays at 25 days showed less than

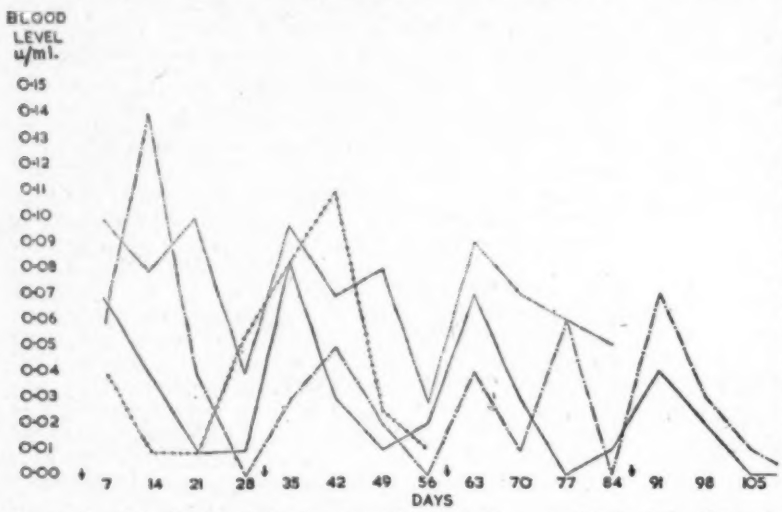
TABLE I.—*Serum Penicillin Concentrations*

	Days after Injection			
	4	11	18	25
Total No. of samples	66	62	58	56
No. with serum concentrations of 0·02 u./ml. and over	66	54	33	15
Range (u./ml.)	0·24–0·025	0·14–0	0·10–0	0·07–0
Av. serum concentration (u./ml.)	0·08	0·043	0·029	0·012

0.02 unit per ml., but in many of these there were still detectable traces of penicillin in the serum. Absorption appeared to be irregular, even in the same child. Thus, after some injections serum levels remained above 0.03 unit per ml. for at least 25 days, while after others no penicillin was detected after shorter periods. The Chart shows the levels found in four children and how they varied in the same child from injection to injection. As noted by Stollerman and Rusoff, most of the injections gave rise to local soreness and tenderness for 24 to 48 hours. No urticarial or other skin rashes were seen. However, in 18 out of 67 injections slight fever was noted on the following day. This ranged from 99 to 100.5° F. (37.2 to 38.1° C.). It did not occur after every injection in the same child.

The "control" group of rheumatic children was made up of 43 children who received no treatment and the 22 "treated" children who were observed for from three to seventeen weeks before starting treatment. Seventeen of these were group A carriers on admission and yielded persistently positive swabs, without a change of type, throughout their period of observation, for from four to twenty weeks. Twenty-two had persistently negative swabs through-

out their periods of observation, which varied from four to 21 weeks. The remainder in the control group gave one or more positive swabs intermittently, and often with a change of type, presumably as a result of cross-infection. Only one of these infections was accompanied by clinical signs or symptoms—that is, complaint of sore throat with three days' pyrexia.



Curves showing the blood levels of penicillin (units per ml.) in four different children at weekly intervals after 1.5 mega units of benzathene penicillin. Arrows indicate the times of injections. Detectable penicillin of less than the minimum assayable value is shown as 0.01 unit per ml.

Effect of Treatment

Group A streptococci were eliminated within four days from the throats of all but one of the 15 persistent carriers in the treated group. In the one exception, group A streptococci of the same type as he started with were isolated from the patient at the second and third swab after his first injection, and then disappeared. As a result of this effect of treatment the load of infection, which had been very high at the beginning of the study, fell after July 1 (Table II).

TABLE II.—*Numbers of Swabs which Yielded Group A Streptococci*

	Rheumatic Patients				Orthopaedic Patients Untreated	
	Treated		Untreated*			
	Total	Positive	Total	Positive	Total	Positive
March			87	35		
April			99	30		
May			131	69	28	8
June			87	44		
July	43	1	75	37		
August	59	3	42	10		
September	51	0	39	5	26	10
October	51	0	53	7	31	6
November	27	0	51	15		
December	12	0	45	8		
January	7	2	49	11	20	7
February	9	0	45	10	19	5

* Includes patients subsequently treated.

Hence, in order to compare the rate of occurrence of infections among treated and control patients it was necessary to consider separately the initial period, before any treatment was given, and the period July 1 to February 28. A new infection was shown by the isolation of a group A streptococcus from a throat which was previously negative, or which had previously carried a different type. However, as it was possible that a few of the patients carrying group A streptococci had more than one type in their throats at the same time, and as only one colony was picked for testing from each positive plate, there had to be a gap of at least one negative swab before accepting the isolation of a new type as evidence of infection in a patient who had previously carried Group A streptococci.

In estimating the infection rates, differences in times of exposure to the infective environment were allowed for by relating the number of infections (as defined above) to the total number of throat-weeks at risk. When a patient yielded a positive swab his throat was not regarded as being again at risk unless it became negative for at least one swab. Thus, for example, if three patients with initially negative swabs had been observed for a period of six weeks, and if two of them had yielded positive swabs at the second and fourth weekly swabbing respectively and had stayed positive subsequently, there would have been two infections in 12 throat-weeks, giving an infection rate of 16.7%. The average infection rate in all the rheumatic children observed between March 1 and June 30, 1953 (before any treatment was given), was 6.6%. Between July 1, 1953, and February 28, 1954, the rates in the control and treated groups were respectively 2.9% and 0.37% (Table III). The fall in the infection rate among the control patients after July 1 was presumably caused by the lessening of the load of infection in the whole community.

Throughout the study the penicillin sensitivity of every culture of group A streptococcus was tested by a filter-paper strip method. In no case was resistance found to be greater than that of the Oxford staphylococcus.

TABLE III.—*Group A Streptococcus Infection Rates in Treated and Untreated Rheumatic Fever Convalescent Children*

	March to June, 1953			July, 1953, to Feb., 1954		
	Total Swabs	Positive Swabs	%	Total Swabs	Positive Swabs	%
Load of infection in community (including orthopaedic patients)	532	186	35·0	754	137	18·2
	Infection Rate					
	Throat-weeks at Risk	No. of Infections	Rate %	Throat-weeks at Risk	No. of Infections	Rate %
Untreated patients	196	13	6·6	312	9	2·9
Treated "	0	—	—	270	1	0·37

Conclusions

Monthly intramuscular injections of benzathene penicillin in doses of 1.5 mega units produced prophylactic blood levels of penicillin in the majority of children.

These injections gave rise to some local tenderness for 24 hours, and in some cases slight fever.

These injections eliminated group A haemolytic streptococci from the throats of carriers, and almost completely prevented new infections.

We are indebted to Mr. L. J. Waller for much technical assistance and to Dr. R. E. O. Williams for typing the streptococci. Our thanks are also due to John Wyeth and Brother Ltd. for a generous supply of benzathene penicillin (" penidural "), without which the investigation would not have been possible.

ADDENDUM.—Since this study was completed one child developed a group A streptococcal sore throat 25 days after an injection of benzathene penicillin and subsequently developed a relapse of rheumatism.

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USE OF A RECORDING DYNAMOMETER IN CLINICAL MEDICINE

BY

W. RITCHIE RUSSELL, C.B.E., M.D., F.R.C.P.
F.R.C.P.Ed.
Department of Neurology, United Oxford Hospitals

There are many occasions in clinical medicine when the study of muscle strength and function is important. Disorder of the motor functions may be reflected in different ways, many of which are amenable to some system of recording.

Simple recording dynamometers have been used in this clinic during the past three years, and have been referred to in connexion with studies of muscle recovery in poliomyelitis (Russell, 1952). The machine used was designed by Dr. E. H. J. Schuster (later models have been made by H. G. East and Co., Longworth Road, Oxford) and is illustrated in Figs. 1 and 2. Two or more strengths of spring are available, and the maximum grip which can be recorded is 90 lb. (41 kg.). The normal grip is occasionally greater than this but will soon fatigue below the maximum figure on sustained contraction. The recording paper is moved by clockwork, and two speeds are available. Both hands may be tested together, with the recording pens (ball-pointed) side by side or one above the other.

Examples of Records Taken

Such records may be of value in following the course of a paretic condition from day to day, but a single record is often informative, and may demonstrate varieties of motor disorder of which the following are examples.

All records read from left to right. When both hands are tested together the record of the right hand is either to the left of or above the left, and may overlap it to a varying extent according to the particular machine used. The records may be taken by asking the patient to make a maximum contraction with both hands and to "hold it" while the recording pens are concealed from the patient by holding a sheet of paper in front of his eyes. Another type of record is obtained by asking the patient to make rapid repeated contractions. Sometimes each hand is tested separately.

Fig. 3 gives the appearance which may be taken as normal for a maximum contraction maintained for about 80 seconds, and illustrates a normal fatigue curve.

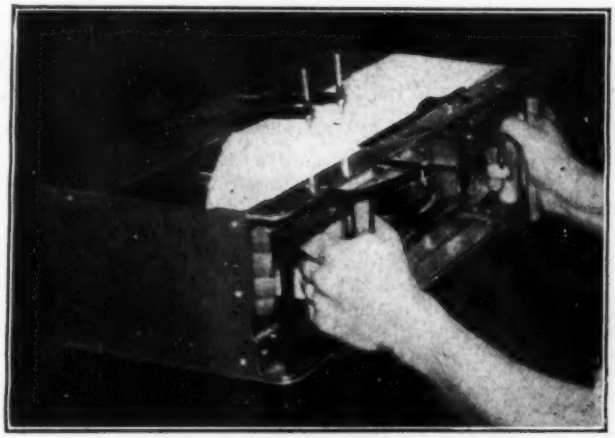

FIG. 1.—Recording dynamometer in use.

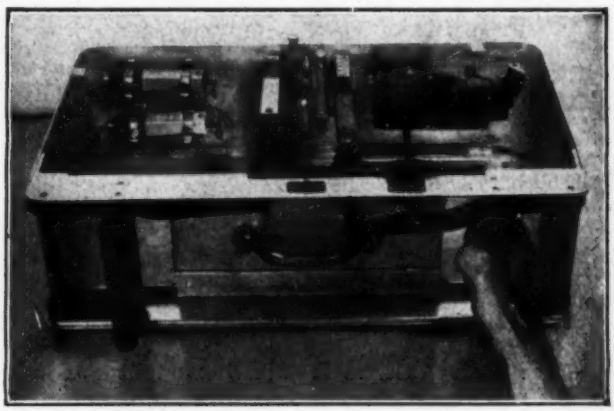

FIG. 2.—Dynamometer with top plate removed to show design.

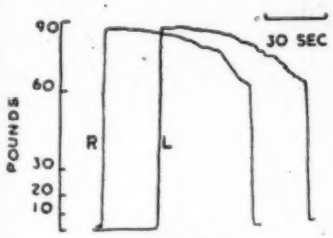

FIG. 3

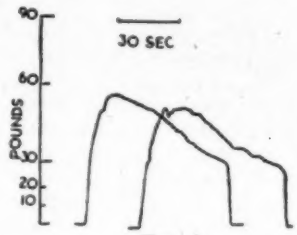

FIG. 4

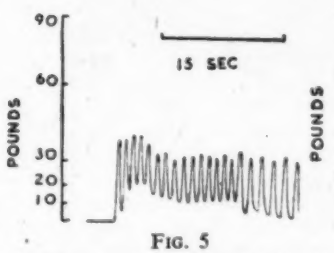

FIG. 5

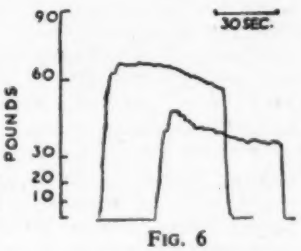

FIG. 6

FIG. 3.—Normal: both hands recording together. R=right; L=left. FIG. 4.—Slight myasthenia. FIG. 5.—Myotonia congenita. FIG. 6.—Small lesion of the right parietal lobe.

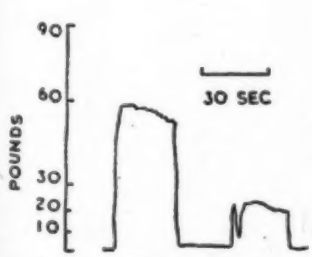

FIG. 7

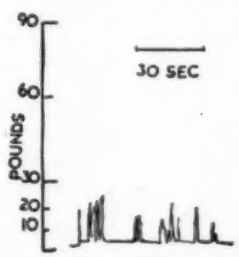

FIG. 8

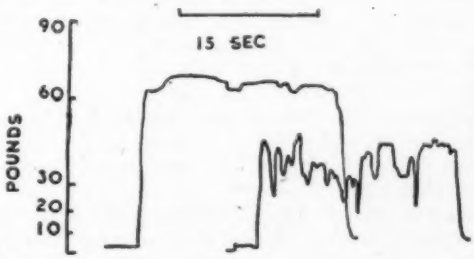

FIG. 9

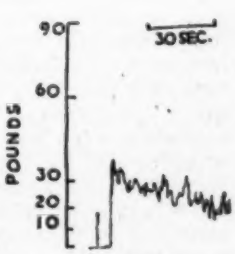

FIG. 10

FIG. 7.—Right frontal tumour. FIG. 8.—Rheumatic chorea. FIG. 9.—Left hemiballismus. FIG. 10.—Congenital choreo-athetosis.

Disease of Muscle.—Fig. 4 gives the record of a slight case of myasthenia gravis in which fatigue develops more rapidly than normal. Fig. 5 is from a patient with myotonia congenita who made repeated maximum contractions. The failure of full relaxation is well seen in the early part of the record, and then "works off."

Hysteria and Malingering.—Functional weakness of one hand is common, and repeated records with the dynamometer have much value in diagnosis and treatment. The record obtained may also be of legal value in compensation cases. Hysteria and malingering are indistinguishable from each other. Fig. 13 shows practically no movement of the hysterical right hand and a normal curve for the left. Fig. 14 is somewhat similar, but here there is also some interference with contraction of the normal hand (left). Contraction with the left hand alone, however, was quite normal. Repeated records have sometimes helped to clarify the disability when there is a mixture of organic disease and hysteria. The types of curve obtained in various psychological conditions have not been investigated further, but might well prove to be fruitful.

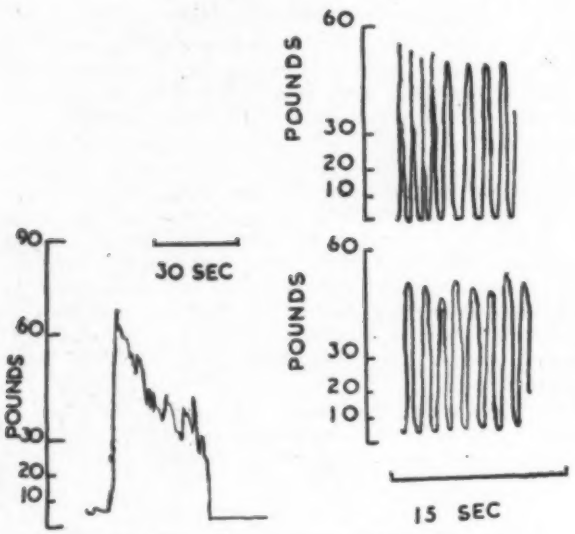

FIG. 11 FIG. 12

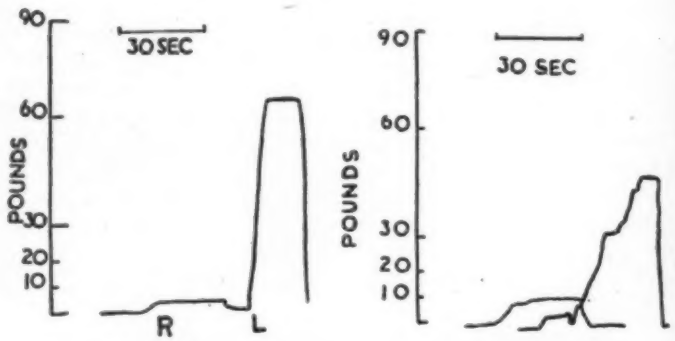

FIG. 13 FIG. 14

FIG. 11.—Wilson's disease. FIG. 12.—Early parkinsonism on right (upper). FIG. 13.—Hysterical paralysis of right hand (R). Left grip (L) unaffected. FIG. 14.—Hysterical paralysis of right hand: left grip also hesitant.

Focal Cerebral Lesions.—Focal lesions of one or other cerebral hemisphere may lead to contralateral paresis which is slight and can only be demonstrated by some mechanical device. Fig. 6 illustrates the effect of a small cerebral thrombosis in the right parietal lobe for which slight astereognosis of the left hand was the only obvious sign. Fig. 7 was the tracing produced by a patient with a right frontal tumour causing adversive fits. Lateralizing signs were inconspicuous and the recorded degree of weakness of the left grip surprised those in charge of the case.

Disorders of Motor Functions.—Dynamometer recordings of motor disorders give many interesting pictures of the various forms of disintegration of motor function. In unilateral cerebellar lesions the dynamometer demonstrates some paresis, and, in addition, the record of rapidly repeated contractions is more slow and irregular than on the normal side. Remarkable records are obtained in patients with chorea. Fig. 8 is the record of a child of 10 years with severe rheumatic chorea attempting to grip steadily, but sudden relaxations are very frequent and make sustained contraction impossible. In cases of Huntingdon's chorea the same characteristics are present to a lesser degree, and Fig. 9 shows a somewhat similar feature from a case of left hemiballismus in a patient aged 70 caused by a vascular lesion in the right subthalamic region. Cases of congenital spastic diplegia with choreo-athetosis also give a tracing of this pattern (Fig. 10). Fig. 11 is recorded by a young man severely disabled by Wilson's disease: it shows a failure to maintain the grip and the irregularity with sudden relaxations of the type seen in chorea. Fig. 12 is from an early case of Parkinson's disease affecting the right side only. There is little difference between the two hands as regards maximum strength and speed of repeated contractions, but the tracing shows a distinct slowing and irregularity of the change from relaxation to the next contraction on the affected side. Severe disorders of motor function can also be demonstrated in advanced cases of disseminated sclerosis. Rapid weakening of the initial maximum contraction is often a striking feature of these cases and is mingled with a varying degree of irregularity of the tracing.

Such recording devices are also useful in the clinical study of rheumatic conditions, not only for recording the degree of loss of function but also for identifying the added psychological disability which is often present in arthritic diseases.

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The second edition of the Unesco *Directory of International Scientific Organizations* (H.M.S.O., price 13s. 6d. net), published a short time ago, is a useful reference book for the scientist of whatever discipline. Two hundred and sixty-four organizations are described, classified under the three main headings: "Basic Sciences, Applied Sciences, and Miscellaneous," "Agricultural Sciences, Engineering Sciences, and Medical Sciences," and lastly "Miscellaneous," a group which includes organizations whose activities either enter into a number of different scientific fields or, while not being entirely scientific, are of interest to scientists. Under the Medical Section there are listed 76 international and 16 regional organizations. Where relevant, the following information is given about each organization: official name and address; nature and aims; governing body, officers, and membership; commissions set up within the organization; special facilities such as laboratories, research centres, or libraries; financial resources; meetings and voting; publications; relations with other international organizations; short history and bibliography; any useful supplementary information. The manuscript of the *Directory* was completed by the end of June, 1953, but the *Directory* itself was not on sale in Britain until the middle of May, 1954. This has naturally dated some of the information about meetings and officials, but it does not seriously diminish the usefulness of the *Directory*.

EFFECT OF HYPOTHERMIA ON THE HYPOTHALAMIC–PITUITARY RESPONSE TO STRESS

BY

H. H. KHALIL, M.B.

(From the Department of Pathology, Guy's Hospital Medical School, London, S.E.1)

While it is now established that the functions of the neurohypophysis are controlled by nuclei in the hypothalamus, the mechanisms that regulate the various activities of the adenohypophysis remain obscure. In spite of its independence of any immediate neural control, the adenohypophysis is still capable of adjusting its activities promptly to the varying demands of the body. The almost immediate mobilization of endogenous A.C.T.H. following minor stress stimuli (Sayers and Sayers, 1947) suggests that a reflex mechanism is playing a part in this response. Further evidence for this hypothesis was recently recorded by Porter (1953), who observed that in cats lesions in the posterior hypothalamus block the pituitary–adrenocortical response to stress. When the lesions were made more anteriorly they were ineffective. Porter's observations show that certain functions of the adenohypophysis may also be mediated through the hypothalamic nuclei. Yet despite the many studies the pathway(s) taken by the agent(s) that regulate the activities of the adenohypophysis is (are) still unknown.

The present experiments were carried out to examine the effect of marked lowering of the body temperature on the pituitary–adrenocortical response to stress stimuli. Such hypothermia might selectively depress any neural participation in the release of A.C.T.H. by the adenohypophysis. Evidence is given below to show that with a degree of hypothermia of about 20° C. the adrenal cortex remains responsive to parenteral administration of small doses of A.C.T.H.

Materials and Methods

Sixty-eight male albino rats of inbred Wistar strain and weighing 80–100 g. were used. After keeping them in a room thermostatically controlled at 24° C. for several days they were divided into five groups and treated as follows.

Group I.—After the left adrenal gland had been removed under ether anaesthesia the animals were allowed to recover from its effects for twenty minutes. They were then transferred to a cold room at 0° C. and kept there for thirty minutes. On their return to the laboratory they were re-anaesthetized, their rectal temperature recorded, and preparations made for the removal of the remaining adrenal, which was excised sixty minutes after the first.

Group II.—These rats were treated in the same way as those in Group I except that they were not transferred to the cold room between the two operations.

Group III.—These rats were treated in the same way as those in Group II except that the anaesthesia was maintained for the whole sixty minutes between the two operations.

Groups IV and V were taken in batches of six at a time. They were rapidly anaesthetized with ether and transferred to the cold room. Open ether anaesthesia was maintained during the period of chilling. The rectal temperature of each animal was recorded throughout the experiment. While in the cold room the anaesthetized animals were unable to maintain their body temperature, which fell rapidly in twenty-five to thirty minutes to about 20° C. (animals that fell to lower temperatures were discarded). They were then returned to the laboratory and placed prone on a grid 1 in. (2.5 cm.) above a large block of ice. The anaesthesia was maintained by occasional open ether. The rectal temperature was maintained at 20–21° C. throughout the experimental period. The respiration rate ranged between 20 and 30, and the heart rate was about 120 a minute. Left adrenalectomy was performed forty minutes after starting the anaesthesia, when the animals were hypothermic. This unilateral extirpation was immediately followed by the injection of adrenocorticotrophin (A.C.T.H., Armour, K55908) in N/30 acetic acid into the tail vein of Group V animals. Doses of 1/500 and 1/250 I.U. were administered to Groups Va and Vb respectively. The same volume of N/30 acetic acid was injected into Group IV animals. The remaining adrenal gland was removed sixty minutes after the first.

Each adrenal gland was dissected free from fat and weighed to the nearest 0.1 mg. Its ascorbic acid content was estimated by the method of Roe and Kuether (1943) as modified by Sayers *et al.* (1948). Colorimetric measurements were made with a Spekker absorptiometer.

Results

The response of these animals to the stresses of anaesthesia, adrenalectomy, and chilling was judged by the degree of ascorbic acid depletion of the second of their adrenal glands; each animal thus acts as its own control. The comparative effects of each of these stressing agents are shown in Table I, from which the following conclusions

TABLE I.—*Comparative Effects of the Stress Induced by Various Combinations of Adrenalectomy, Anaesthesia, and Chilling*

Group	No. of Animals	Treatment	Mean Rectal Temperature	Ascorbic Acid Content (mg. per 100 g. of Fresh Tissue)		
				1st Gland	2nd Gland	Difference
I	10	Adrenalectomy +chilling	33° C.	440±18	230±13	−210±22
II	8	Adrenalectomy	35° C.	447±15	272±16	−175±17
III	8	Anaesthesia + adrenalectomy*	33° C.	410±19	230±12	−180±22
IV	22	Chilling under anaesthesia prior to adrenalectomy*	20·5° C.	390±10	396±10	+6±14

* Anaesthesia is mentioned only when maintained throughout the experiment.

can be drawn: (*a*) That in Groups I and II the operation alone brought about a great and significant fall in the ascorbic acid content of the second gland. This fall was rendered even more severe by the added stress of chilling. (*b*) That the similarity in the fall in the ascorbic acid content in Groups II and III shows that the maintenance of

TABLE II.—*Response of the Adrenal Cortex in Hypothermia to the Intravenous Injection of A.C.T.H.*

Group	No. of Animals	Stress	A.C.T.H.	Mean Rectal Temperature	Ascorbic Acid Content (mg. per 100 g. of Fresh Tissue)		
					1st Gland	2nd Gland	Difference
IV	22	Chilling under anaesthesia prior to adrenalectomy*	—	20·5° C.	390±10	396±10	+6±14
Va	13		1/500 I.U.	20·5° C.	370±13	318±14	−52± 8
Vb	5		1/250 „	20·5° C.	392±29	323±26	−69± 8

* Anaesthesia is mentioned only when maintained throughout the experiment.

anaesthesia throughout the experiment does not mitigate the pituitary–adrenocortical response to the operative stress. (c) That a comparison of the very different changes in the ascorbic acid content in Group IV and the other three groups shows the extent to which the pituitary–adrenocortical response is inhibited by hypothermia.

Further experiments were carried out to determine the degree of responsiveness of the adrenal cortex in hypothermia to varying doses of A.C.T.H. These results are shown in Table II. It will be seen that with a degree of hypothermia of about 20° C. the parenchymatous cells of the adrenal cortex are still sensitive to small doses of A.C.T.H., though there is no linear relationship between dosage and loss of ascorbic acid. Moreover, the response in hypothermia is sluggish when compared with that of hypophysectomized rats at normal temperatures.

Discussion

The rapid fall in the ascorbic acid content in the adrenal glands of animals exposed to various kinds of stress has led to its use for quantitative biological assay of adrenocorticotrophic activity (Sayers *et al.*, 1948). Though the significance of the disappearance of this vitamin is little understood, its loss has been widely recognized as a satisfactory quantitative assay method for A.C.T.H.

The fall in the ascorbic acid concentration in the second adrenal gland in Groups I, II, and III was the expected response of these animals to the various combinations of the stresses imposed by anaesthesia, adrenalectomy, and exposure to cold. When the stresses were imposed on animals that were already hypothermic, as in Group IV, they failed to show any depletion in the ascorbic acid content of the second gland. This implies that at this lowered body temperature the pituitary–adrenocortical mechanism was inhibited. That this inhibition was not due to the effect of the maintained anaesthesia is shown by the response of Group III animals, which were kept anaesthetized throughout the experiment. Nor could it be attributed wholly to lack of sensitivity on the part of the adrenal cortex, for Group V animals showed that with this degree of hypothermia the adrenal cortex still shows some response to small doses of A.C.T.H.

It can be concluded from these findings that at this degree of hypothermia the adenohypophysis does not release any appreciable amount of A.C.T.H. in response to the stresses applied. Whether this block is due to an inhibition of certain metabolic activities in the adenohypophysis or to the interruption of a neural or neurohumoral phase in the response mechanism is not clear from the present experiments. The evidence of hypothalamic involvement in the pituitary–adrenocortical response to stress (Porter, 1953) favours the view that, in hypothermia, an inhibition of neural transmission of stress stimuli is mainly responsible for this block. The study of the effects of hypothermia on the stress response may be a useful guide to the further understanding of the mechanism involved.

Summary

Evidence is given to show that in hypothermic rats the hypothalamic–pituitary mechanism leading to the release of A.C.T.H. in response to stress stimuli is inhibited. The adrenal cortex in such chilled animals, however, remains responsive to the intravenous injection of small doses of A.C.T.H.

I should like to thank Mr. J. R. Young for his technical help and co-operation.

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A SIMPLE METHOD OF RAISING AND LOWERING BODY TEMPERATURE

BY

H. H. KHALIL, M.B.

AND

R. C. MacKEITH, D.M., F.R.C.P.

(From the Departments of Pathology and Child Health, Guy's Hospital, London)

While studying the effects of stress in hypothermic rats it was noted that at a body temperature of 20° C. the pituitary response was inhibited and that of the adrenal cortex was much reduced (Khalil, 1954). With these small animals changes in body temperature could be effected readily; when dogs and rabbits have been made hypothermic, rewarming by the external application of heat takes much longer than with rats, and this delay may have contributed to the death of some of the animals. The introduction of warm water into the stomach could provide a simple and rapid method for supplying heat to the body, since the stomach wall is highly vascularized and lies close to the aorta, vena cava, portal vein, and other large vessels. Conversely, by using cold water a marked degree of hypothermia can be attained.

Since repeated changes of cold or warm water are needed to effect the desired temperature changes, the water is introduced through a tube which joins a rubber balloon lying in the lumen of the stomach. By this procedure the water remains "external" to the body and any loss of electrolytes by gastric lavage or excessive absorption of water is avoided.

The apparatus used consisted of a thin "portex" plastic tube with a finger-stall, which on inflation could readily hold 250 ml., tied securely to one end. The other end was attached to a two-way tap connected with a 50-ml. syringe and with a rubber inlet tube from the warm or cold water to be used. The temperature of the former is about 40° C. and of the latter about 4° C. The irrigation was carried out once every five minutes, each change of water remaining in the balloon for about three minutes. The method was employed for rabbits and was effective in lowering the rectal temperature to about 25° C. in two hours and to 20° C. in three hours and in raising it to normal again in about four hours. The heart rate was slowed from 240 to 60 beats per minute. This work will be reported more fully later.

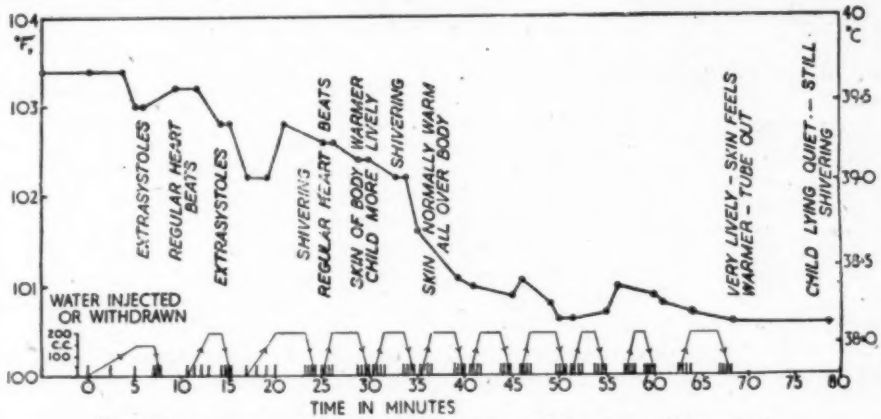
At this stage an opportunity arose of using this method for cooling a 16-months-old child with hyperpyrexia who had not responded to the usual methods of cooling.

Case History

A boy aged 16 months was admitted to hospital on June 29, 1954, with pneumonia, which resolved with treatment. There was a family history of fits, and the boy had had severe fits at 10 months while teething. On the first and second day after admission he had fits and was left with a right hemiparesis and regression in general behaviour to that of a 10-months-old child, although he was alert and active. On July 15 he was transferred to Guy's Hospital, and on July 16 an arteriogram was done which showed slight shift of cerebral vessels to the left. On the morning of July 20 he had a temperature of 104° F. (40° C.); no abnormality was found in the throat, ears, lungs, and urine. At 1 p.m. he was stuporous and very ill, with cold skin

and a rectal temperature of 105° F. (40.6° C.). Despite repeated cold applications for five hours the temperature did not fall below 103.5° F. (39.7° C.).

The intragastric balloon devised for rabbits was passed with ease. After 150 ml. of water at 32–39° F. (0–4° C.) had been introduced slowly over five minutes, the rectal temperature began to fall (see Chart). Some extrasystoles were noted. After staying two minutes in the stomach, the 150 ml. was withdrawn; its temperature was about 80° F. (26.7° C.). Between the 11th and 13th minute after



Graphical representation of cooling the child on the first occasion.

starting cooling a further 200 ml. of ice-cold water was injected, extrasystoles being noted again towards the end of the injection. After one and a half minutes this was withdrawn. Between the 17th and 20th minute 200 ml. of water (making a total of 550 ml.) was injected. At the 21st minute the temperature rose to 102.6° F. (39.3° C.). During the next 26 minutes, five further changes of 200 ml. each were given. Despite this faster rate of exchanges no further extrasystoles were detected either by auscultation or by intermittent E.C.G. records, even immediately after filling the stomach with ice-cold water. At the 29th minute the temperature was 102.4° F. (39.1° C.), and the skin of the body felt warmer.

At the 30th minute the patient began to awake from his stupor and to protest. Salivation was noted from this time on. At the 32nd minute he began shivering. By the 37th minute the body, arms, and legs felt warm (except over the stomach, where the skin felt icy cold). At the 50th minute the temperature was 100.6° F. (38.1° C.); three further lots of 200 ml. of water were injected and withdrawn during the next 18 minutes without further fall in temperature. At the 68th minute the child was very lively and the skin felt normally warm. His general condition was greatly improved and the tube was withdrawn. A total of 2,150 ml. of water had been introduced and withdrawn.

About four hours after stopping the intragastric cooling the rectal temperature had risen again to 103.6° F. (39.8° C.) and the boy had relapsed into stupor with cold, pale, greyish skin of the trunk and limbs. The tube and rubber bag were reintroduced. During the next hour twelve changes each of 200 ml. of cold water at 32–39° F. (0–4° C.) were made. As a result the body temperature fell from 103.6° F. (39.8° C.) to 100.6° F. (38.1° C.). By the 32nd minute he had woken sufficiently to cry and move about; satisfactory improvement in circulation and body temperature took longer on this occasion, for it was not observed until an hour after cooling had been started. The tube was removed at the 65th minute. At the 75th minute the child was taking milk by mouth with good appetite. He has kept well and has remained apyrexial.

Discussion

In experimental work on hypothermia, difficulties arise during the rewarming stage after a marked lowering of the body temperature has been produced. As has been learnt in treating men exposed to severe cold, warming by external application of heat to the body surface may have serious disadvantages. The warmed peripheral tissues may increase their metabolic demands before the blood supply is adequate. Moreover, if the capillary bed of the skin opens before the general circulation has improved, there will be a fall in blood pressure. Rewarming by the intragastric route avoids these troubles. Furthermore, the skin circulation of the hypothermic animal, including man, is so reduced that little heat may be conveyed from the warmed skin. By internal warming, heat is applied to the vascular gastric mucosa and to the great vessels close to the stomach; their circulation is never stagnant. This method has further theoretical advantages which may prove to be important. It seemed to one of us (H. H. K.) that if the liver could be warmed first, then heat would also be gained from the various metabolic activities of this important organ. Furthermore, an "active" liver would be better able to meet the increasing metabolic demands of the body during warming.

As regards cooling, much of the above discussion applies. The method has proved practicable for rabbits and for a child. It has the advantages over arteriovenous and venous methods that it does not involve opening any blood vessels or cooling the blood to such low temperatures that the dissociation of its oxyhaemoglobin becomes seriously impaired (Barcroft and King, 1909–10).

The success of the intragastric method in the case of this child is an example of the possible applications in clinical medicine. Warming is needed for patients suffering from exposure to cold or occasionally in refrigeration plants. On the other hand, cooling may be required for patients suffering from heat stroke or hyperpyrexia in the course of infective and cerebral diseases. A marked degree of hypothermia is also indicated on occasions in operative surgery.

Although the application of the method to a child was successful, some modifications of the procedure used suggest themselves. (1) Salivation was profuse as revival began and atropine might be given with advantage. (2) Extrasystoles were observed in the early stages of cooling. These might be avoided if the first changes of water were not ice cold. They, however, did not continue, although the rate of introduction of fresh changes of cold water was increased. (3) By fitting two catheters into the intragastric balloon further advantages could accrue. The reduction of temperature of the intragastric contents could be made gradual; this could be easily controlled if the balloon were fitted with a thermocouple. The continuous flow achieved by using two catheters would make a more rapid exchange of water possible. This improvement would probably increase considerably the rate of temperature change, a step which might be necessary in adults.

An approximate calculation may be made of the exchange of heat in the child. Though the water introduced was drawn from a reservoir containing melting ice, it is probable that in passing through the tubing and syringe held in the operator's hand it was slightly warmed. It may be assumed that it was at about 4° C. on entering the stomach. In the first cooling of the child the temperature on withdrawal was as follows:

150 ml. ..	80° F. (26.7° C.)	200 ml. ..	60° F. (15.6° C.)
200 ml. ..	70° F. (21.1° C.)	200 ml. ..	60° F. (15.6° C.)
200 ml. ..	68° F. (20.0° C.)	200 ml. ..	66° F. (18.9° C.)
200 ml. ..	64° F. (17.8° C.)	200 ml. ..	62° F. (16.7° C.)
200 ml. ..	64° F. (17.8° C.)	200 ml. ..	65° F. (18.3° C.)
200 ml. ..	65° F. (18.3° C.)		

Warming 2,150 ml. of water from 4° C. to a mean temperature of 19° C. would require about 32 large calories.

The child's weight was 12 kg. The fall in body temperature was 1.6° C., from 103.4° F. (39.7° C.) to 100.6°F. (38.1° C.). Assuming the specific heat of body tissues to be 1, then in this cooling the body would give up 20 large calories. The difference, 12 large calories, probably represents much of the endogenous heat produced and removed during the period of cooling.

Summary

A method of raising and lowering the body temperature in animals and man by the introduction of changes of water into an intragastric bag is described. It has possible applications in the treatment of excessively high and low body temperatures and also in the management of hypothermia in operative surgery.

We wish to thank Professor G. Payling Wright for his advice and helpful criticism, and Dr. D. G. Montefiore, Miss J. R. Tanner, sister in charge of the children's ward, and Miss Sylvia Tredgold, of the department of medical illustration, for their help and co-operation.

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JUSTIFICATION FOR APPENDICECTOMY IN CHRONIC APPENDICITIS

BY

IAIN McLENNAN, F.R.C.S.Ed., F.R.F.P.S.
Surgeon, Out-patient Department, Glasgow Royal Infirmary

AND

J. KENNEDY WATT, F.R.C.S., F.R.F.P.S.
Surgical Registrar, Glasgow Royal Infirmary

The very existence of chronic appendicitis is often a subject of controversy, yet appendicectomy for this condition is one of the most commonly performed surgical operations. Is there any justification for removing the appendix of a young man or woman complaining of pain in the right iliac fossa? An investigation of a large series of cases was undertaken in an attempt to elucidate whether operation had been justified by results.

When appendicectomy is performed in patients suffering from recurrent attacks of pain in the right iliac fossa there is usually very little correlation between clinical, operative, and pathological findings. The removal of an apparently normal appendix may relieve the patient of all symptoms, yet little or no relief may be obtained from the excision of a fibrosed and adherent organ.

The difficulty of assessing the significance of pathological changes in the appendix is well illustrated by the findings of Shelley (1937). He found that 63% of the appendixes removed incidentally in the course of other operations showed inflammatory changes, and that 72% of the appendixes removed for chronic appendicitis showed similar changes, the other 28% being normal microscopically. Further, in an inquiry into the clinical aspects of the condition, he found (1938) that of those patients whose appendixes showed microscopical evidence of disease, 89% could be regarded as cured, but where the appendix was microscopically normal the cure rate was as high as 80%. It would therefore seem that an appendix showing pathological changes is only slightly more likely to be a cause of symptoms than an apparently normal one. It seems equally clear that the presence of inflammatory changes is no guarantee that the symptoms are due to these. Accordingly, fibrosis and adhesions may be more indicative of previous appendicitis than of present symptoms.

The part played by faecaliths in acute appendicitis seems fairly well established (Shattock, 1916), but their importance in chronic appendicitis is less certain. That their presence may be responsible for attacks of appendicular colic is generally accepted, but the frequency of such occurrence is in doubt, as is the significance of faecaliths found at operation. The belief that they do have some importance is supported by Shelley's (1937) findings that where faecaliths formed the only pathological finding the cure rate of appendicectomy was 85%, compared with 74% for appendixes showing no apparent abnormality.

Chronic appendicitis has long been incriminated as a cause of pylorospasm and dyspepsia, and there is no doubt that many cases of dyspepsia are clinically improved by appendicectomy. Whether this is a case of cause and effect or merely the result of the rest enforced by convalescence from the operation is a matter for discussion. That the early benefit conferred on many cases of undiagnosed dyspepsia is considerable and misleading is well exemplified by an article on five such cases written by Moynihan in 1910. The correspondence evoked by this article is illuminating, and a possible result was to induce a spate of appendicectomies in the treatment of dyspepsia which may not have completely subsided yet. Confusion regarding the interrelation of stomach, duodenum, and appendix is also shown in an article by Braithwaite (1942), in which he states that duodenal ulcer is often mimicked by chronic appendicitis and that haematemesis occurs in about 4% of cases of the latter disease. Such a misconception possibly arises from overreliance on the accuracy of radiological diagnosis, which, although reliable in the demonstration of chronic peptic ulcers, is fallible in the elucidation of recurrent minor ulceration.

Radiological examination of cases of chronic appendicitis is not helpful, and generally no specific evidence of disease is procurable. It may, on occasion, enable one to relate tenderness accurately to the appendix, but the main value of barium examinations lies in the exclusion of other pathological conditions of the gastro-intestinal tract.

Present Investigation

In view of certain doubts about the existence and importance of chronic appendicitis, the present investigation was undertaken. All patients operated on for chronic appendicitis in one unit of the Glasgow Royal Infirmary from 1946 to 1950 inclusive were contacted so far as was possible and interviewed. The years 1945 and earlier have not been included, as during the war these cases were dealt with mainly by the hospitals of the Emergency Medical Service, and the years subsequent to 1950 have been excluded to allow an adequate interval between operation and interview. In all, 429 females and 134 males were available for study and 316 females and 97 males were traced, a follow-up of 73.3%. Of those traced, the majority (65%) were personally interviewed and examined by us, and the remainder replied to a questionary.

A certain degree of selection of the cases submitted to operation is bound to have occurred, since these cases were admitted via the out-patient department, but the selection was not unduly rigorous and patients complaining of persistent and recurring pain were usually admitted for operation. The basis of this inquiry, therefore, lies in the assumption that those in whom the diagnosis had been correct would, after operation, remain free from pain; and, conversely, if a similar pain persisted after appendicectomy the diagnosis had been wrong. In many of the latter group

the correct diagnosis had been elucidated by subsequent events or investigations, but where this was not evident a full investigation was undertaken by us before the final classification was made. In many of the cases reviewed slight residual pain remained in the right iliac fossa, but this was regarded lightly by the patients concerned, possibly because, as they stated, it was a considerable improvement on their previous state or because their fear of a severe attack of appendicitis had been removed. Such cases were classed among the "cured" and accounted for 15% of the total cures.

Sex and Age Incidence

In this series females outnumber males in the proportion of 3.2:1, this ratio being higher than that found by other observers—for example, Willauer and O'Neill (1943), 1.6:1; Shelley (1937), 2:1; and Paulson (1950), 2:1. The cure rate for females was found to be 83.5% and for males 74.2%.

If the belief is correct that subsequent freedom from pain is evidence of cure, there would, on the above figures, seem to be a much higher and unexplained incidence of chronic appendicitis in females. On the other hand, if the attempt is made to explain the higher incidence of right-sided pain in females as being due to functional or organic disorders of the pelvic organs, it might be expected that a reasonably high proportion would show evidence of gynaecological complaints at a later date. Rather to our surprise we found that in only 4 of the 316 females traced did the pain appear to have been produced by gynaecological conditions.

As might be expected, the condition occurs mainly in young people, the average age being 24 years in women and 25 years in men. The age distribution (see Chart) is similar in both sexes, the maximal incidence lying between 15 and 30 years of age.

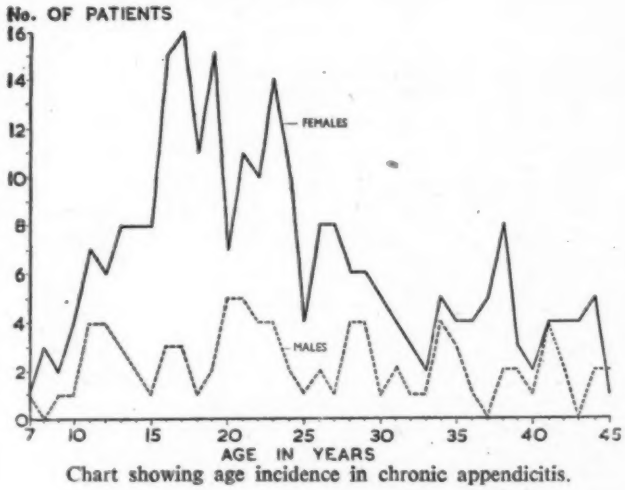

Chart showing age incidence in chronic appendicitis.

Pain in Chronic Appendicitis

Pain was found to be the presenting symptom in every case; it had been present on an average for eighteen months in females and for sixteen months in males. These figures are somewhat elevated by the inclusion of some patients who had had symptoms for many years. In 12.7% of the females and 22.7% of the males symptoms had been present for less than three months.

In the majority (Table I) the pain occurred in the right iliac fossa and was typically recurrent in type, the patient having several episodes of pain at irregular intervals. Rarely could these attacks be identified in retrospect as attacks of subacute appendicitis. The next most common site was the central abdomen, where pain occurred either alone or combined with pain in the right iliac fossa. In the case notes pain was sometimes noted to have occurred in other sites—namely, right hypochondrium, epigastrium, right lumbar region, and right groin—this group of patients accounting for 9.5% of the women and 19.6% of the men.

TABLE I.—*Pain in Chronic Appendicitis*

Site of Pain	No. of Patients	
	Females	Males
Right iliac fossa	240 (75·9%)	61 (62·9%)
Central abdomen and right iliac fossa	46 (14·6%)	17 (17·5%)
Other sites	30 (9·5%)	19 (19·6%)
Total	316	97

When the patients were divided into three groups according to the site of occurrence of pain, and these groups were related to the number of patients cured of pain by operation, the figures shown in Table II were obtained. The occurrence of pain in the right iliac fossa or central abdomen was associated with a high percentage of cures. On the other hand, pain experienced elsewhere was associated with a lower cure rate, this being 60% for females and 58% for males. Accordingly, it would appear that pain in the right iliac fossa or central abdomen is a more reliable guide to diagnosis than pain elsewhere. Furthermore, it would seem inadvisable to accept a diagnosis of chronic appendicitis when the pain is atypical before a full investigation has been carried out.

TABLE II.—*Cure Rate in Relation to Site of Pain*

Site of Pain	Percentage Cure Rate	
	Females	Males
Right iliac fossa	86	77
Central abdomen and right iliac fossa	85	82
Other sites	60	58

Percentages are taken to nearest whole number.

Ultimate Diagnosis

An analysis was made of the actual or probable diagnosis reached in the 52 (16.5%) females and 25 (25.8%) males who continued to complain of pain after operation and were not classed as cured by appendicectomy (Table III).

TABLE III.—*Ultimate Diagnosis in 413 Cases of Chronic Appendicitis*

	No. of Patients	
	Females	Males
Cured	224 } 83·5%	62 } 74·2%
Cured with minimal residual pain	40 }	10 }
Duodenal ulcer	10 (3·2%)	10 (10·3%)
Cholecystitis	6	1
Gynaecological lesions	4	—
Renal lesions	2	2
Mesenteric adenitis	1	—
Ulcerative colitis	1	—
Carcinoma	1 (rectum)	1 (caecum)
Spinal tuberculosis	—	1
Tuberculous enteritis	1	—
Sarcoma of ilium	—	1
Constipation	—	1
Neurosis	8	2
No diagnosis reached	18	6
Total	316	97

The commonest source of error lay in the misinterpretation of symptoms not characteristic of duodenal ulcer, but which, in retrospect, appear undoubtedly to have been due to this cause. This fallacy was greater in males, of whom 10.3% were thought to have been suffering from duodenal ulceration and not appendicitis at the time of operation. This figure is exclusive of those who were known to be suffering from ulcer at the time of operation and of those whose subsequent affliction by ulcer was thought to bear no relation to their appendicitis. This experience emphasizes the need for care in the interpretation of recurring attacks of abdominal pain, a feature of both duodenal ulcer and chronic appendicitis. This fallacy is more likely to occur in the older patient (Table IV), but it can also be a source of error in younger ones, as shown by the presence of duodenal ulcer in two boys aged 12 and 14 years at the time of appendicectomy.

TABLE IV.—*Diagnosis in Relation to Age*

Final Diagnosis	Females		Males	
	Under 30 Years	Over 30 Years	Under 30 Years	Over 30 Years
Cured	193 (86·6%)	71 (76·3%)	52 (83·8%)	20 (57·1%)
Duodenal ulcer ..	5 (2·2%)	5 (5·4%)	4 (6·5%)	6 (17·1%)
Other diagnoses ..	25 (11·2%)	17 (18·3%)	6 (9·7%)	9 (25·8%)
Total ..	223	93	62	35

Great care in the taking and interpreting of the case history is necessary and sometimes vital, as can be seen by the varied assortment of final diagnoses which resulted. The danger is that a more serious condition might be missed rather than that an unnecessary appendicectomy might be performed. In the cases of sarcoma of the right ilium and carcinoma of the caecum and rectum which occurred, the correct diagnosis was not made until three to six months after appendicectomy, and vital time was lost before appropriate treatment was carried out.

On the whole, Table III follows the expected lines, though fewer cases of cholecystitis and of gynaecological lesions occurred than might have been expected.

In a small number of cases—namely, 26 females and 8 males—no definite organic lesion could be found to account for the persistent pain. A psychiatrist's assessment of the personalities of this group might differ radically from our own, but we were able to classify only eight females and two males as frankly neurotic, this being considered to be the cause of their complaints. In the remaining 18 females and 6 males no explanation of the cause of the pain is offered.

Mortality and Morbidity of the Operation

No patient in this series died after operation for chronic appendicitis; this accords with general experience, though Shelley (1937) noted four deaths in 881 cases. There is, however, a definite morbidity attributable to the operation as shown by the post-operative complications listed in Table V. Several of these—thrombosis, pulmonary collapse,

TABLE V.—*Morbidity of Operation*

Post-operative Complication	No. of Patients	
	Females	Males
Pulmonary	14	5
Haematoma	4	4
Wound sepsis	9	4
Phlebo-thrombosis	1	1
Tonsillitis	2	—
Enteritis	2	—
Pelvic abscess	1	—
Major rectal haemorrhage	—	1
Incisional hernia	1	—
Pericaecal haemorrhage; paralytic ileus; faecal fistula	—	1
Total	34	16
Percentage morbidity	10·8	16·5

and wound sepsis—are possible hazards of any surgical operation, but others such as pelvic abscess, major rectal bleeding, and faecal fistula were more surprising. The occurrence in one unfortunate patient of pericaecal haemorrhage followed in turn by paralytic ileus, faecal fistula, and incisional hernia indicates that convalescence from the operation is not always uneventful.

With regard to any late morbidity of the operation, it was found that three women who had had no further abdominal pain complained rather bitterly of disabling headaches dating from, and presumably attributable to, the use of spinal anaesthetics. They thought the exchange had not been a fair one. Four other women complained of dysmenorrhoea which dated from the time of appendicectomy.

The Incision.—The incision most commonly employed in this series was the muscle-splitting or grid-iron approach; this was used in 90% of the cases. As might be expected, the cure rate when a paramedian incision was employed (60%) was lower than that when a grid-iron incision was used (83%), which merely reflects the pre-operative diagnostic doubt in the former cases.

The removal of the appendix in chronic appendicitis is probably best performed through a grid-iron incision, which gives minimal disturbance to the patient and a short convalescence. Such an approach, which permits of only a limited abdominal exploration, is justified by the high cure rates recorded here, and by Shelley (1937), 87% in 704 cases, and by Davis (1927), 76% in 420 cases. In some cases, especially in older patients, an abdominal exploration through a paramedian incision would appear to be preferable. Although in the majority no gross abnormality would be revealed, the occasional demonstration of more serious lesions would justify the routine use of a paramedian incision in patients over 40 years of age.

Conclusion

As Shelley (1939) was forced to conolude that chronic appendicitis is a clinical entity, we suggest that the findings of this investigation provide ample justification for appendicectomy in patients who have recurrent attacks of pain in the right iliac fossa or central abdomen. Good results are to be anticipated in the great majority of cases.

The operation, however, is never an urgent one, and undue haste can be productive of serious errors. Time should be spent in assessing the patient's disability, and all appropriate investigations must be carried out.

Examination by barium meal would seem to be desirable in men over 30 years of age. Its routine use over the past few months in such cases has already yielded positive results for duodenal ulcer in patients with very atypical pain.

Summary

The results of a follow-up of 413 cases of appendicectomy for chronic appendicitis are presented.

Females preponderated in a proportion of 3.2:1 and most patients were aged between 15 and 30.

The overall cure rate was 83.5% for females and 74.2% for males.

Duodenal ulcer proved to be an important fallacy in the diagnosis of chronic appendicitis.

We wish to thank Mr. John Dunbar for the facilities granted us to pursue this investigation and for his encouragement throughout.

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A manual for the guidance of laboratory workers concerned with rabies has just been published by W.H.O. (Monograph Series, No. 23; 150 pp., 51 illustrations; price £1). Fourteen rabies specialists from various parts of the world have contributed papers on five aspects of rabies research technique: laboratory diagnosis, methods of vaccine production, vaccine-potency tests, the production of hyperimmune serum, and the care and breeding of experimental animals. The monograph is not an exhaustive treatise: its aim is to present selected procedures which would be dependable and practicable. It is abundantly illustrated, and a list of general reference sources complements the specific references given in each of the 19 sections. Although the present speed of development in rabies research indicates that modification of some of the techniques described will eventually be necessary, it is thought that they will prove a useful guide for several years to come.

Medical Memoranda

Unusual Case of Hydatid Cyst of the Brain

The following case is interesting because of the rarity of primary hydatid cysts of the brain, and because no symptoms were present until eight hours before death. The distribution of primary hydatid cysts in children is as follows: liver, 76.2% ; lung, 11.1% ; brain, 4.3% (as against 0.7% in adults). The reason for this is the relatively large size of the carotid arteries in children. The peak incidence in children is at the age of 11 years. Normally such cysts produce local and general symptoms. I was fortunate in that I saw the child in her home, almost as soon as any symptoms developed, and was able to remain with her practically continuously in hospital until her death.

CASE REPORT

At 8.30 a.m. on February 17, 1953, I was called to see a girl aged 3½ who had had a sudden onset of vomiting and several convulsions during the previous hour. For three days she had had a slight cough and cold, but otherwise was perfectly well. She had woken up at about 7 a.m. and appeared perfectly normal until the onset of the vomiting a little later.

Physical examination showed a pale ill-looking child. She was having slight convulsions almost continuously, with pronounced convulsive movements of the right arm. She lay on the left side with the left elbow and knee flexed, and both the left arm and leg had continuous twitching movements. Her temperature was 100.2° F. (37.9° C.), and pulse 100. Marked nystagmus of the eyes to the left and rigidity of the neck were present. The knee and ankle reflexes were increased and brisk, the abdominal reflexes were absent.

The child was admitted to hospital and kept under observation. Lumbar puncture showed colourless C.S.F. under considerable pressure. The report on this fluid was as follows: clear colourless fluid ; white cells, 8 per c.mm. ; films of deposit showed scanty red blood cells and lymphocytes ; no organisms were seen ; sugar present ; globulin not in excess ; protein, 20 mg. per 100 ml. ; culture yielded no growth after 24 hours ; chlorides 700 mg. per 100 ml.

By 11.30 a.m. the temperature was 104° F. (40° C.), and pulse 110. The convulsions continued and the child passed water automatically. In spite of repeated tepid sponging the temperature continued to rise. At 2 p.m. it was 107.8° F. (42.1° C.), pulse imperceptible. In an attempt to lessen the convulsions 4 ml. of paraldehyde was given intramuscularly at 2.40 p.m. The temperature was then 105.2° F. (40.7° C.), pulse still imperceptible. At 3 p.m. the temperature was 105° F. (40.6° C.), and her condition was much worse. At 3.30 p.m. the temperature was 104.8° F. (40.5° C.), the pulse still imperceptible. The limbs continued to twitch, and the position of flexion of the left arm and leg was maintained. At 3.40 p.m. the child died.

Post-mortem Examination.—The body was that of a well-developed female child, with no external evidence of disease or injury. Brain: a large whitish cyst about 8 cm. in diameter was present arising from the dura and pressing upon the left parietal and frontal lobes ; the brain substance itself was not involved ; the cyst was leaking an opalescent fluid; the cyst wall contained a smooth outer surface studded with whitish papules ; much free fluid was present. All the other organs were normal, except that the mesenteric lymph nodes were enlarged and somewhat inflamed. Examination of the fluid taken from the cyst within the brain showed numerous scolices of *Tinea echinococcus*. The cause of death was rupture of the large echinococcus cyst in the brain due to hydatid disease.

Subsequent questioning of the parents regarding the child's previous health and behaviour over the past two years showed that they had noticed that her reaction to pain was quite abnormal. Injuries and hurts had no effect on her at all, and she appeared to be immune to any pain sensations. When told the cause of death, they stated that before they had moved to their new house they had lived in rooms where the owner had a greyhound which died of worm infection in August, 1951. They had moved in December, 1951. Casoni's intradermal test was carried out on the parents and their son, aged 5½, all of which were negative.

COMMENT

This case was unusual in nearly every way. Primary hydatid cysts of the brain are rare, though they are more common in children than adults. In this case the age of the child was well below the average age of incidence. The sudden onset of symptoms in the presence of such a large cyst was exceptional, there being no symptoms presenting presumably before rupture of the cyst. The time between their onset and the child's death was so short that a diagnosis was practically impossible, and the child's condition deteriorated with extreme rapidity.

My thanks are due to Dr. David Heuspear, who carried out the post-mortem examination.

P. L. RHODES, M.R.C.S., L.R.C.P.,
Non-resident Hospital Medical Officer,
Bridgnorth and South Shropshire Infirmary.

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Lipogranuloma of the Peritoneum

Lipogranuloma of the peritoneum is now a complete rarity, and the occasional isolated example is a reminder of the once common practice of introducing oily substances into the peritoneal cavity in an attempt to minimize or prevent primary and especially recurrent adhesions, to delay toxic absorption in peritonitis, and to facilitate peristalsis. Such a substance, no matter how bland and chemically inert it appears to be, is treated as a foreign body, and after a variable time and in varying degree produces fibrosis, adhesion formation, and granulomatous masses, so that the end-result is a condition worse than that which it was hoped to prevent. After reading the extensive literature on the experimental work with regard to adhesion prevention, it is surprising to find so few recorded examples of this condition which can readily mimic malignant disease.

CASE HISTORY

A married woman aged 60 complained of recurrent epigastric pain and vomiting. In 1931 hysterectomy was performed for fibroids, but no records could be traced. In 1933 she developed abdominal symptoms, and a laparotomy was performed by the same surgeon, when "a ? neoplastic necrotic mass was found which on section showed fat and cellular endothelial tissue not malignant." A laparotomy was carried out at a London teaching hospital in 1939. "Two tumours, one at umbilical level and the other 3½ in. (9 cm.) below it, were found in the posterior rectus sheath and macroscopically were typical carcinomatous deposits. An attempt to open the peritoneal cavity was abandoned owing to dense adhesions. No biopsy was taken."

The patient first came under my care in March, 1941, and a further laparotomy was performed. "There was a palpable mass in the epigastrium moving on respiration. The anterior abdominal wall, pelvis, and peritoneum were full of secondaries. There was a mass proximal to the pylorus but no pyloric stenosis. A palliative gastro-enterostomy was done." From 1941 she had attacks of epigastric pain and vomiting, lasting about two weeks and occurring every two to six months. The pain was severe, spread downwards, occurred at any time, not being related to meals, and could last all day. The vomiting might last up to 12 hours and the vomitus was dark and bile-stained. Her appetite was fair. There had been a slight weight loss recently. She tended to be constipated.

On examination a very thin woman with atrophic abdominal skin and sunken eyes (long-standing) was seen. There was no anaemia. Hard tender nodules were felt in the right iliac fossa, in the pouch of Douglas, and a hard mass was present between the pubis and umbilicus.

Investigations.—A barium-meal examination showed no abnormality except the gastro-enterostomy. Multiple calcified ring shadows were noted, particularly in the right iliac fossa and pelvis but extending up to the left subphrenic area (Fig. 1). The radiologist suggested the diagnosis of peritoneal paraffinomata.

FIG. 1.—X-ray film of abdomen, showing the calcified ring-like shadows. Note the single large gall-stone lying between the transverse processes of lumbar vertebrae 4 and 5.

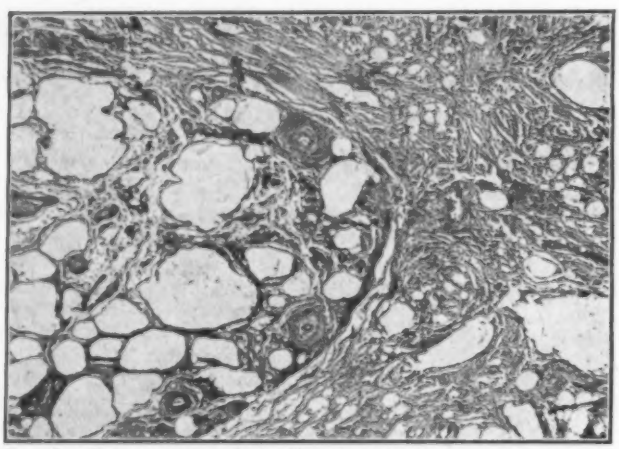

FIG. 2.—Photomicrograph (×28) of part of a granuloma, showing the oil spaces, fibrosis, and endarteritis.

The earlier diagnosis was undoubtedly wrong, but it was difficult to suggest a likely one. An undiagnosed perforation with gross soiling of the peritoneum and later foreign-body reaction around the larger particles was considered together with some unusual form of peritonitis, perhaps tubercular in origin or due to talcum powder.

At laparotomy in May, 1952, multiple dense adhesions were found, rendering abdominal exploration difficult. Numerous calcified nodules were present in the mesentery and on the bowel wall and parietal peritoneum. Other greyish-yellow and softer nodules proved to be fibro-fatty tissue. Two larger ones were opened and contained clear oily fluid, resembling liquid paraffin. No mass was found in the stomach. Eight days later a further attack of vomiting and abdominal pain occurred, possibly due to the large gall-stone (Fig. 1), which was later confirmed by cholecystography.

Pathological Report.—Sections showed a chronic non-suppurative inflammatory reaction based on a foreign-body reaction to an oily material which may well be liquid paraffin. The specimen of oil was very small, but did not char on applying concentrated sulphuric acid, showing that it was mineral and not vegetable in origin (Fig. 2). The liquid paraffin was presumably introduced at the hysterectomy in 1931. This could only have been used in the hope of preventing primary adhesions, there being no proof that she was predisposed to adhesion formation.

DISCUSSION

This story again emphasizes the importance of histological confirmation of malignancy before giving a hopeless prognosis. Biopsy in 1939 or 1941 would probably have given the correct diagnosis, despite the apparently overwhelming evidence of malignancy.

The radiological picture is highly characteristic, but not well known. These ring-like calcified shadows lying mainly in the pelvis but scattered irregularly throughout the abdomen are seen in only one other condition—pseudomyxoma peritonei. Sometimes the shadows are not circular but mulberry-like or with a serrated margin. They vary in size from 1 to 3 cm. Even in pseudomyxoma peritonei calcification is an unusual finding and presumably requires a fairly long time for its development. Calcified uterine fibroids and echinococcal cysts do not bear a close resemblance because they are usually restricted in their situation and number, although hydatid cysts, which are generally larger, may occur throughout the mesentery.

The usual cause of symptoms is recurrent intestinal obstruction, but in this case it is possible the more recent attacks were related to the gall-stone—a useful reminder not to overlook the commonplace when caught up in the excitement of a rare condition, although cholecystectomy would have been very difficult in this case.

Interest in adhesion formation and its possible prevention or limitation quickly grew once abdominal surgery had become established. A great deal of experimental work was performed without consistent results and in the belief that oily substances were harmless and non-irritating. Later work refuted these earlier claims and showed the experiments had not lasted long enough to allow the described sequelae to develop.

Busch and Biebergeil (1908) showed that paraffin which is liquid at body temperature is slowly absorbed and irritating, while that which is solid is not absorbed and acts as a foreign body. Liquid paraffin as used therapeutically is a mixture of hydrocarbons of varying melting-points, and this variation may help to explain the differing experimental conclusions and the fact that not all patients develop large granulomata.

I wish to thank Mr. R. A. Fitzsimons for permission to publish this article, Dr. C. D. T. Maclean for his expert radiological opinion, and Dr. W. E. Evans for the histological report.

A. R. MAKEY, M.S., F.R.C.S.,
Lately Senior Surgical Registrar,
Charing Cross Hospital.

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Reviews

HIDDEN CAUSES OF DISEASE

The Hidden Causes of Disease. By Antonio Benivieni. Translated by Charles Singer. Biographical Appreciation by Esmond R. Long. (Pp. 217; illustrated. 50s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954.

Professor Charles Singer has once more laid everyone interested in the history of medicine under a debt of gratitude to him for his scholarly translation of the pioneer work of Antonio Benivieni on the hidden causes of disease. Mr. Esmond Long has added a biographical appreciation. The Latin text is beautifully reproduced and is faced by the corresponding English translation. On page 119 the proof-reader has failed to detect a lack of correspondence between the Latin and English versions.

Antonio Benivieni was termed by Jean Cruveilhier "the father of pathological anatomy," and we are here correctly told that this book "stands out among medical books as the first one to give extensive consideration to the practice of post-mortem examination." Benivieni lived from 1443 to 1502, and during his lifetime printing was introduced, so that this book, which was printed in 1507, was one of the earliest, if not the earliest, of printed books in which clinical records and post-mortem examinations are correlated.

Among over a hundred clinical cases here recorded it is easy to recognize many well-known conditions, such as tetanus, osteomyelitis of the fibula, hernia, gall-stones, Ludwig's angina, hysteria, ileus, cancer of the stomach, hypospadias, and haematocolpos. On the other hand, in many cases the details do not permit of any diagnosis. Surgeons had their difficulties in those days. We are told that, when the obstructing membrane causing the haematocolpos was incised, "at once such a profuse and violent flow of blackish matter came out that the lamp which my assistant was holding near was extinguished."

On another occasion when Benivieni was treating a man suffering from enormous abdominal distension by the application of a cupping glass to the navel "the unity of the navel was loosed [that is, it burst] and a quantity of wind burst out and dashed the cupping glass to pieces."

Case XII, which is called "water under the skin," appears to have been due to ascites, for we read that the "navel was loosed and the water began to gush out with so much force that it rose to the height of three cubits above the belly."

Case LV recounts the strange cure of an architect, one Nicolo, who "fell headlong from a high tower, but so far from being hurt thereby he thenceforth walked in a normal manner, though before he had gone with a limp."

Particular interest attaches to Case XXXIII, in which the cause of death was said to be an abscess on the mesentery. When the reader notes, however, that the patient was a boy otherwise healthy who suffered from severe abdominal pain which continued for several days until he died, and that at necropsy the viscera were found to be normal, but when removing the intestines an abscess was opened from which there flowed out "a quantity of blackish fetid matter like encaustic blacking," he will wonder whether this was not in fact a case of abscess due to a perforated gangrenous appendix.

This book, which preceded the work of Morgagni by 150 years, should make an immediate appeal to all clinicians and pathologists and, of course, to everyone interested in the history of medicine.

ZACHARY COPE.

BIOCHEMISTRY

Textbook of Biochemistry. By Benjamin Harrow, Ph.D., and Abraham Mazur, Ph.D. Sixth edition. (Pp. 563; illustrated. 32s. 6d.) Philadelphia and London: W. B. Saunders Company. 1954.

What was originally "Harrow and Sherwin" and then became "Harrow" has now, in the sixth edition, become "Harrow and Mazur." It is a classic textbook of its kind, and has been used by many generations of medical students throughout the world. It continues to represent a less dynamic approach to the subject than do some more recent textbooks of biochemistry, which pivot largely on the intracellular enzyme system to the neglect of the "building stones." "Harrow and Mazur" gives us something of everything, and for this reason will often appeal to the medical student, for whom a dynamic approach alone is insufficient.

This new edition has been extensively revised, and such topics as paper chromatography have appropriately been introduced. The discovery of the pancreatic hyperglycaemic–glycogenolytic factor (H.G.F.; glucagon) is incorrectly ascribed to Funk and others, although particulars of the publications of these authors on this topic, given in the fifth edition, are now omitted. Harington's name is misspelled on page 479, and recent important work on the significance of triiodothyronine is not mentioned. But it is never difficult for a reviewer to disagree with an author's handling of particular sections in such a general textbook, and on the whole this book steers a steady and reliable course between the dangers of extremes.

To have produced an edition which is nearly 10% smaller than the last but still covers the growing field of biochemistry in its own fashion is a feat of which the authors may well be proud. The result is an eminently readable book containing many useful references to recent literature. Medical students will certainly continue to use it, and others will doubtless find in it much of interest and value.

F. G. YOUNG.

SOCIAL SCIENCE AND MEDICINE

Social Science in Medicine. By Leo W. Simmons and Harold G. Wolff. (Pp. 254. $3.50.) New York: Russell Sage Foundation. 1954.

In this book, under the joint authorship of a sociologist and a physician, it is argued that medicine has much to gain from an alliance with the social sciences. This is a view which has been expressed frequently in recent years, and it rests on two assumptions: that the social environment influences the origin or course of many diseases, and that the social sciences have developed methods appropriate to investigation of the social component in aetiology.

About the first of these assumptions there is unlikely to be much disagreement. Simmons and Wolff discuss work in the social sciences, chiefly in the field of cultural anthropology, to illustrate the significance of the social and cultural environments in relation to health. A considerable part of their book is devoted to an examination of "links between stress and disease," of which they quote examples drawn largely from the well-known work of Professor Wolff and his associates.

It is about the usefulness of some of the methods currently employed in the social sciences that there are likely to be differences of opinion. Although the authors make no exaggerated claims—indeed their book is commendably restrained on a subject which seems to invite loose statements—they apparently subscribe to the view that understanding of the aetiology of disease can be advanced by close collaboration between medical and social scientists. It is easy to say that one disagrees with this view, but difficult to explain why within the space of a short review. But it is probably not unfair to regard as characteristic of the sociologist's

approach a discussion of the aetiology of peptic ulcer (page 129). It is suggested that a change in the sex ratio of patients admitted to the New York Hospital with a perforated ulcer (from a ratio of 7 males to 6 females in 1900 to one of 36 males to 3 females in 1939) may be associated with the emancipation of women, which is among the changes which "can be viewed as undermining the established statuses and emotional supports for man." The biologist is likely to regard this as the kind of statement that is best left unrecorded until it can be supported by evidence. And he may feel that, before attempting to apply the findings of social scientists to the complex problems of the aetiology of human disease, he would be well advised to do his own thinking.

THOMAS MCKEOWN.

RHEUMATOID ARTHRITIS

Klinik und Therapie des Chronischen Gelenkrheumatismus. By Professor Dr. Karl Fellinger and Dozent Dr. Josef Schmid. (Pp. 614+ix; 222 figures and 55 tables. $10.80.) Vienna: Wilhelm Maudrich. 1954.

This is a most remarkable volume which sets out to record virtually everything that has been written about certain aspects of rheumatoid arthritis. The authors are still under the influence of Klinge's unitary concept of an all-embracing "Rheumatismus." As a result the histological changes they present are mainly those of rheumatic fever, which are not strictly relevant, but fortunately this lack of definition is largely avoided in the rest of the book.

The treatment of aetiological theories, laboratory findings, and therapy are particularly thorough. There are separate chapters on treatment by hormones, gold salts, salicylates, pyrazole derivatives, and "neural therapy" which includes everything from spinal pumping to intravenous procaine; and each chapter is followed by a bibliography of 200 to 1,300 references. The chapters dealing with clinical features and differential diagnosis are relatively sketchy but still monumental. There is, however, no chapter on the general management of the patient and little discussion of such important matters as rest and exercise, plaster splintage, and operative treatment, which seems a curious omission.

The authors rarely express an opinion about the merits or demerits of the work they quote and so leave the reader to make his own choice between the various theories of pathogenesis and conflicting therapeutic claims: this detracts from the value of the book to the general physician, but the rheumatologist who wishes to delve into the literature about some special aspect of rheumatoid disease will find much precise information and a wealth of references. This is essentially a book to consult rather than a book to read, but as such it is thoroughly recommended.

J. H. KELLGREN.

PITFALLS IN SURGERY

Fehler und Gefahren bei chirurgischen Operationen. Edited by R. Stich and K. S. Bauer. Volumes I and II. (Vol. I: Pp. 742; 133 illustrations. Vol. II: Pp. 743–1396; 76 illustrations. D.M. 61.) Jena: Gustav Fischer. 1954.

The title of this great work—"Mistakes and Dangers in Surgical Operations"—gives very little idea of its scope and value. The words should have been added, "And how they may be avoided by skill and knowledge." Here are gathered the experiences of more than twenty of the greatest German surgeons, described with rare candour and most accurate detail, placing at our disposal a volume of ripe judgment to which it would be difficult to find a parallel.

Each article starts with the proper assumption that the reader is fully conversant with the subject, and the discussion deals at once with the difficulties which may arise and the abnormalities which may be encountered. Thus in dealing with the gall-bladder a full description is given of the many variations which occur in the ducts and in the vessels and of how these variations may lead even the most cautious surgeon into trouble. Moreover, recovery from a mistake is fully discussed and expert advice is given on what is perhaps one of the most difficult and perplexing situations in surgery. Again, in thyroidectomy the dangers of injury to the intercurrent laryngeal nerve and to the parathyroid glands are well known, but the abnormalities which may lie concealed and lure the most careful operator into trouble are here set out in full detail in a study of the greatest practical value to the surgeon. Indeed, the wider his experience the greater will be his appreciation.

The whole field of surgery, including the brain and the thorax, is covered in the same thorough manner, and every page is full of ideas with all the freshness of personal experience. In addition there is a monumental bibliography fully up to date and admirably arranged. For the young surgeon the book is a gold-mine, but we venture to think that the most experienced will still read it with pleasure.

HENRY SOUTTAR.

75 YEARS OF MEDICINE

Seventy-Five Years of Medical Progress, 1878–1953. Edited and with a foreword by Louis H. Bauer, M.D., F.A.C.P. (Pp. 286; illustrated. 30s.) London: Henry Kimpton. Philadelphia: Lea and Febiger. 1954.

This book is the result of a conference of the Western Branch of the World Medical Association which was held in Richmond, Virginia, in April, 1953, to commemorate 75 years of medical progress. Men in 20 specialties, including general practice, were invited to contribute papers on the history and the present status of their particular fields in medicine. The results are somewhat uneven in so far as some have concentrated on history, and others on present status, and without being parochial one can say that this is not such a good book as *Fifty Years of Medicine*.

As in a number of recent American books, the articles on general practice, rehabilitation, and psychiatry are the most interesting to the British reader. Bryner has written an interesting essay suggesting that medicine has completed a cycle and is coming back to the recognition of the general practitioner as the central figure, whose specialty is the whole patient; he notes that over 35% of the general hospitals in the U.S.A. now have departments of general practice in operation. Rusk gives statistics for the rise in chronic illness and the consequent increased need of physical rehabilitation in an ageing population. Bartemeier points out how and why American psychiatry became psycho-analytically orientated during the second world war. The book is well produced and not unreasonable in price, but the insertion of photographs of each of the writers gives it a flavour of the works magazine or the advertising brochure.

L. J. WITTS.

Among new editions of important works recently published is Dr. Maurice Davidson's *A Practical Manual of Diseases of the Chest* (Oxford Medical Publications, 84s.). The preface tells us that this is the fourth edition in eighteen years, and the introduction of modern chemotherapy has necessitated many alterations. In addition, a number of old illustrations have been replaced by fresh ones.

An account of "the more everyday application of biochemistry to the problems of clinical medicine" is given by Dr. C. P. Stewart and Professor D. M. Dunlop in their *Clinical Chemistry in Practical Medicine* (E. and S. Livingstone, 4th edition, 21s.). The book has been thoroughly revised and is intended for the general medical reader.

In the second edition of their comprehensive survey of *Blood Groups in Man*, Drs. R. R. Race and Ruth Sanger have incorporated an account of work published since the first edition came out four years ago. This includes the new blood group system, *Kidd*. Nine systems are now defined. The book is published by Blackwell Scientific Publications for 30s.

A third edition has appeared of Dr. E. W. Caryl Thomas's book *A Synopsis of Forensic Medicine and Toxicology* (John Wright and Sons, 12s. 6d.). The author has revised it to take account of changes made by the National Health Service Acts and other recent legislation.

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AIR DISINFECTION IN SCHOOLS

One of the major medical research efforts early in the war was aimed at finding a means of preventing the air-borne spread of infection. Many feared that epidemics would break out in Service barracks and training camps as well as in the highly unhygienic conditions in air-raid shelters. An account of the substantial British contribution to this study was given in the Medical Research Council monograph, *Studies in Air Hygiene*.[1] Unfortunately its conclusions were far from encouraging, at least as regards the feasibility of widespread adoption of any of the methods studied. The chemical agents tried included resorcinol, sodium hypochlorite, which was considered to have a limited sphere of usefulness, and lactic acid and related compounds: these last were remarkably active, but, like triethylene glycol, which was in the meantime being extensively studied in the United States, they have not provided a solution to the outstanding problem.

The main alternative to chemical disinfection is irradiation with ultra-violet light, and this was shown to be effective, with the exception that it fails to kill bacteria in dust particles and thus requires to be combined with dust-suppression measures. Ultra-violet irradiation is in fact the only one of these various methods the study of which has been constantly pursued until the present time on both sides of the Atlantic. It can be used in three ways, two of which are specialized and restricted to hospitals: these are the provision of "curtains" of light at the entrance to ward cubicles[2] and the irradiation of the field of a surgical operation advocated by Hart.[3] If entire rooms are to be irradiated the lamps must be suspended above head level and the occupants protected from direct light; thus only the upper stratum of the air is subjected to bactericidal irradiation. That this is nevertheless of some value seems to be shown by studies made in the United States, particularly in schools, where the spread of infectious disease has been diminished,[4] but also in infant nurseries,[5] and in hospitals.[6]

A Medical Research Council report[7] now gives an account of an extremely thorough study of the effects of indirect ultra-violet irradiation in schools in the borough of Southall during the years 1946–8. The Air Hygiene Committee of the Council is responsible for the report, although in the planning of the investigation representatives of the Ministry of Health, local authorities, and other bodies also took part. Six of the seven primary schools in Southall were used in the investigation, three being controls and three irradiated. Lamps were fitted and run continuously during school hours throughout the three-year period not only in class-rooms but in dining-halls and even in some corridors. The effects were judged by comparison of sickness rates, which are analysed in great detail; and direct observations were also made on the bacterial content of the air at various times by slit samplers.

The effect of irradiation on total air counts was small, but there was an overall reduction in the counts of *Str. salivarius* of 70%, and of 80% in counts of haemolytic streptococci made over a shorter period. It thus seems that mouth bacteria, presumably recently expelled and contained in droplet nuclei, are substantially affected. On the other hand, the effect on sickness incidence was unimpressive. Total absence rates—450 absences per 100 child-years in the irradiated schools and 446 in the controls—did not differ significantly, and differences only became apparent when causes of absence were considered individually. Illnesses distinctly less common in the irradiated schools included mumps, asthma, gastro-enteritis, acute pharyngitis and tonsillitis, and otitis media and earache, and in the infant department scarlet fever and chicken-pox. On the other hand, it appears that these diseases accounted for only a small proportion of the total absences. Another hopeful feature was a substantial reduction in secondary attack rates for measles, chicken-pox, and to a less extent mumps. This corroborates findings in the United States, where the spread of measles and chicken-pox has repeatedly been found to be diminished by irradiation. In view of these facts, and despite the finding that some causes of absence were unaccountably commoner in the irradiated schools, it may seem surprising that no over-all benefit was achieved. By far the commonest causes of absence were acute nasopharyngitis, "ill-defined symptoms," and "non-medical reasons," and it seems that the effect of these and other banal causes on total absence rates tends to obliterate any

[1] *Special Report Series, Medical Research Council, No.* 262 1948, London H.M.S.O.
[2] Robertson, E. C., Doyle, M. E., and Tisdall, F. F., *J. Amer. med. Ass.*, 1943, 121, 908.
[3] Ibid., 1941, 117, 1610.
[4] Wells, W. F., Wells, M. W., and Wilder, T. S., *Amer. J. Hyg.*, 1942, 35, 97.
[5] Rosenstern, I., *Amer. J. Dis. Child.*, 1948, 76, 193.
[6] Barenberg, L. H., Greene, D., Greenspan, L., and Greenberg, B., in *Aerobiology*, published by the American Association for the Advancement of Science, 1942.
[7] *Special Report Series, Medical Research Council, No.* 283, 1954, London, H.M.S.O.

diminution in the incidence of specific diseases. The final conclusion of the report is:

"The effect of irradiation on total sickness absence is therefore small, and the results would not appear to justify wide use of irradiation as a hygienic measure for the control of infection in primary urban day schools."

It will be generally agreed that these results do not justify the expense of applying this method generally. On the other hand, the principle underlying the verdict in this report is not the only one on which a policy might be based. A reduced total absence rate cannot apparently be attained, but constant attendance is no more important than future health, and it seems that something of value may have been achieved, if only in diminishing the incidence of streptococcal sore throats and their complications, particularly middle ear disease.

LONG-ACTING PENICILLINS

Penicillin compounds with different properties are becoming numerous, and their identity cannot be deduced from the various names given to each by manufacturers. It may therefore be helpful to define the properties of those compounds the virtue of which is prolonged action. This is largely a function of solubility: the lower this is the slower will absorption be, although particle size and the vehicle also influence the rate of absorption to a less extent. All the simple penicillin salts—sodium, calcium, and potassium—are highly soluble, and produce the high initial concentrations succeeded by a rapid fall to zero which have long been recognized as the characteristic effect of penicillin in solution, or "aqueous" penicillin. All slowly acting forms are suspensions of a solid, and the first of them, an equimolecular compound of penicillin and procaine, has now been in general use for six years or more. A moderate dose of a good procaine penicillin preparation will exert a continuous effect—that is, maintain in the blood a concentration inhibitory for fully sensitive bacteria—from one day to the next. Larger doses may act for rather longer, but if a continuous effect for several days is desired it may be preferable to use the N-benzyl-β-phenylethylamine salt of penicillin (benethamine penicillin), tests of which were recently reported in this *Journal* by Nelson, Talbot, and Binns.[1] A dose of 300,000 units of this compound was constantly effective for three days, and some subjects had penicillin in the blood after four days: larger doses gave a five-day effect, but without much higher initial levels. This compound has yet to be tested therapeutically, although it will doubtless produce results in conformity with these data, and further experience will show whether local reactions such as were seen in a few of these test subjects, and also noted by one of our correspondents this week (p. 756), are a material drawback.

The longest-acting compound of all has now been known for three years, and has been much more extensively studied. This is N,N′-dibenzylethylenediamine penicillin (benzathine penicillin). Given by injection, this substance exerts an effect for from seven to 28 days or even longer: the duration varies with the dose, but also in different subjects. Fletcher and Knappett,[2] who reported the first pharmacological study in this country, found that, although in some subjects penicillin was still detectable in the blood a month after a dose of 600,000 units, in others negative tests, sometimes intermittent, began to be obtained after one week. A valuable use for such a preparation is evidently the prophylaxis of rheumatic fever. Stollerman and Rusoff[3] gave doses of 300,000–1,200,000 units at intervals of one to four weeks to 143 rheumatic subjects, and showed both that these doses kept penicillin in the blood continuously in the majority of these patients and that they eliminated haemolytic streptococci from their throats. Professor C. Bruce Perrry and Dr. W. A. Gillespie describe a similar study in this issue (p. 729). They gave 1,500,000 units monthly to 22 rheumatic children. The rate of absorption was irregular, as others have found, and 18 and 25 days after a dose only a little over one-half and one-quarter of the blood assays showed detectable penicillin. Nevertheless Group A streptococci were eliminated from the throats of treated children, and the proportion of carriers in a control group of 43 contacts also fell steeply, an interesting finding which is attributed to the "lessening of the load of infection in the whole community." If sulphonamides are to be abandoned for this purpose, monthly injections of benzathine penicillin should replace them: the alternative, oral penicillin, is far more costly and probably no more dependable.

Benzathine penicillin given orally has no such prolonged effect—it has in fact to be administered four times a day—but was said by Bayne and his colleagues[4] and by Cathie and MacFarlane[5] to be better and more regularly absorbed than other forms of the drug. This conclusion was contested in two subsequent papers: Foltz and Schimmel[6] compared the effect of equal oral doses of procaine, potassium, and benzathine penicillin, and found that the first two not only persisted in the blood as long as the last but attained higher levels. A similar superiority of a buffered tablet of potassium penicillin over benzathine

[1] *British Medical Journal*, 1954, **2**, 339.
[2] Ibid., 1953, **1**, 188.
[3] *J. Amer. med. Ass.*, 1952, **150**, 1571.
[4] *Amer. J. med. Sci.*, 1953, **225**, 190.
[5] *British Medical Journal*, 1953, **1**, 805.
[6] *Antibiot. and Chemother.*, 1953, **3**, 593.
[7] *J. Lab. clin. Med.*, 1953, **42**, 417.
[8] *Prescribers' Notes*, 1954, **1**, 74.

penicillin was found by Wright, Purcell, Kass, and Finland.[7] Also to be taken into account in this connexion is the fact that oral benzathine penicillin is considerably more expensive than equivalent doses of *B.P.* sodium or potassium penicillin oral tablets or of procaine penicillin by injection.[8]

ALCOHOLISM AND ATTEMPTED SUICIDE

The suicide rate in Britain, though not high compared with the rate in other Western countries, has risen slightly after a decline during the war. That rise has been due to the increased incidence of suicide among older people.[9] There are also indications that abuse of alcohol is again becoming more common, although in this country, happily, alcoholism and its sequelae are still much less frequent than they were up to and during the 'twenties.[10] It is still possible to work for many months in a busy psychiatric admission ward without seeing a case of delirium tremens, so familiar a picture to the older generation of psychiatrists. However, this state of affairs may not last, and there is need for vigilance as well as research in this field. Conditions for the study of such social phenomena as alcoholism and suicide, and their interrelationship, might be even more favourable in a country where they have not reached the dimensions of a national calamity than in communities where this has happened. Batchelor,[11] in a recent clinical investigation, found that of 200 consecutive cases of attempted suicide admitted to an Edinburgh general hospital, 21.5% (male 32.6%, female 12.0%) had been excessive drinkers and another 8%, although not addicted to alcohol, had been drunk at the time of the attempt. Those who may think that equally high figures are unlikely to be found south of the Border will be disillusioned by Glatt's[12] observations from a mental hospital in Greater London. Stengel[13] found a much smaller proportion of alcoholics among patients admitted as a result of suicidal attempts to a London mental observation ward in 1946, but his case material was probably different from that admitted to a general hospital. More recent comparable American figures[14] closely correspond to those of Batchelor. They are still moderate by comparison with those found by Dahlgren[15] at Malmö, where 46% of males admitted as a result of suicidal attempts were alcoholics. Batchelor's group of alcoholics who had attempted suicide differed in several respects from unselected samples of persons who have made suicidal attempts; among the alcoholics the over-sixties were not the most heavily represented group, as is the case among suicidal attempts and suicides in general. Needless to say, men preponderated among the alcoholics, but women otherwise invariably outnumber men among those who attempt suicide. In this respect, the representation of the sexes among alcoholics who attempt to commit suicide is similar to that found among people who have succeeded in doing so.

The relationship between the incidence of alcoholism and that of suicide is obviously much more complex than was thought in the last century, when Bandel's law of the parallelism of male mortality and the incidence of alcoholism was accepted in many quarters. Nevertheless, Shimshony,[16] working in Switzerland, which has a very high rate both of alcoholism and of suicide, found a significant correlation between alcohol consumption and male mortality in general, and mortality from suicide in particular. At any rate, chronic alcoholics are much more heavily represented among attempted suicides than among suicides, but there is reason to believe that they have a greater proneness to actual suicide than have the average of those who attempt suicide. Stengel[13] has put forward a strong plea for a separate study of those who have attempted suicide and those who have committed suicide. In his view, they represent two different though overlapping populations. This appears to be true of alcoholics. For the psychopathologist there remains the interesting question why so many alcoholics, who indulge in what Menninger[17] called "chronic suicide," should proceed to acts of direct self-injury, most of which do not result in death. This is one of the problems of the economics of aggression which are but little understood.

[9] Swinscow, D., *British Medical Journal*, 1951, **1**, 1417.
[10] Pullar-Strecker, H., *Lancet*, 1952, **1**, 555.
[11] *J. ment. Sci.*, 1954, **100**, 451.
[12] *British Medical Journal*, 1954, **2**, 303.
[13] *Proc. roy. Soc. Med.*, 1952, **45**, 613.
[14] Schmidt, E. H., *et al.*, *J. Amer. med. Ass.*, 1954, **155**, 549.
[15] *On Suicide and Attempted Suicide*, 1945, Lund.
[16] *Schweiz. med. Wschr.*, 1941, **71**, 1429.
[17] *Man Against Himself*, 1938, London.

RENAL TUMOURS IN CHILDHOOD

With the exception of embryoma (nephroblastoma, Wilms's tumour), which is one of the commonest malignant tumours of young children, neoplasms of the kidney are rare in childhood. In a recent review of 70 cases of renal tumours in children, Scott[1] classed 61 as embryomas; 2 others may have been embryomas, and 5 were not primary renal neoplasms. This indicates the overwhelming preponderance of embryoma among kidney tumours in children, and its extremely lethal character gives it urgent clinical importance. Other renal neoplasms, such as the teratoma and the haemangioma reported by Scott, are of interest chiefly as rarities. Renal carcinoma is almost unknown in children. Other, commoner, renal swellings are usually either hydronephrosis or cysts of developmental, not of neoplastic, origin.

The embryoma arises from the mesenchyme of the metanephrogenic blastoma, from which the renal cortex is developed. In the tumour primitive mesenchyme may proliferate as undifferentiated cells or may form epithelial tubules and glomerular structures, as well as fibroblastic connective tissue, and, by aberrant differentiation, other mesoblastic tissues not normally present in the kidney, of which striped or plain muscle fibres are the most usual. Often much of the tumour is wholly undifferentiated, and when microscopical examination is inadequate an erroneous diagnosis of sarcoma or anaplastic carcinoma may be made.

[1] *Glasg. med. J.*, 1954, **35**, 33.
[2] *Abdominal Surgery of Infancy and Childhood*, 1941, p. 424. Philadelphia.

The embryoma is highly malignant and grows rapidly, producing an enormous mass, often with cystic spaces and haemorrhages. It remains for a time confined within the renal capsule, but ultimately transgresses it and freely invades its surroundings. Some kidney tissue usually remains recognizable attached to the tumour. The ureteric pelvis is distorted and compressed or dilated, and may be invaded. Metastasis is mostly by the blood, the chief site being the lungs, less often the liver and occasionally bones. Spread by lymphatics to retroperitoneal lymph nodes is also possible.

Most of the cases are seen in children under 4 years of age, not a few in infants under 1 year. It is much less common in older children and very rare in adults. The usual presenting symptom is a palpable abdominal swelling, and the tumour may be very large before it is noticed. Only a minority of patients have haematuria. Although this symptom may call attention to a tumour not yet palpable, it is of ominous significance, since it indicates invasion of the ureteric pelvis and high malignancy. Pain is not a constant symptom. As the other kidney is usually healthy, evidence of impaired renal function is unlikely. Pyelography, especially intravenous, is useful in diagnosis, revealing the characteristic distortion of the pelvis, or an absence of function on the affected side.

Opinion differs on treatment and the usefulness of radiotherapy. The best results seem to be obtained by immediate nephrectomy, followed by radiotherapy. The survival rate is tragically low. A local recurrence or metastasis usually appears within a year; two years' freedom after nephrectomy is generally regarded as the standard of probable cure, though much later recurrences are not unknown. On this standard only 6 of the 61 cases in Scott's review could be claimed as probably cured. Results given by Ladd and Gross,[2] though rather better, represent a survival rate of little more than 25% eighteen months after nephrectomy. For improved results in the future much depends on earlier diagnosis.

ONCHOCERCIASIS

With such unicellular organisms as the bacteria and spirochaetes, in which the established forms retain the morphology of the infective forms, the invasive organisms, having made successful entry into a suitable host, multiply by reproducing their own kind to a level of saturation which is largely independent of the size of the inoculum. In the case of other unicellular organisms such as the protozoa, although the infective forms may differ from the established form, more or less unrestrained multiplication in the asexual cycle produces a saturation which again is independent of the size of the inoculum, provided this is sufficiently large to ensure infection. In both these groups, therefore, a few infective forms produce a very large number of established forms which may lead to saturation of the host with the parasite. Development of infection in the metazoa follows an entirely different pattern. In the helminths, one infective form when implanted develops to produce a single adult worm. Such adults, after mating, may produce a new generation whose development may be arrested within the same host at almost any stage from the egg to a late larval stage, but, except for a very few accidental exceptions, no more adults can accrue than those which were originally implanted as infective forms. Furthermore, it would appear that in certain species, which include *Onchocerca volvulus*, the numbers of the new generation which persist in this stage of arrested development are limited and are related to the number of their parents. It follows that in such helminth infections an enhanced parasitic population can arise only by the implantation of further infective forms and that saturation of the host with the parasite can, in normal circumstances, arise only as a result of long-continued exposure to infection.[1]

In filarial infections—the infective forms of the parasite being transmitted to man by various species of biting flies—the host-parasite relation has previously been assessed on the incidence in the community of those infected. For some years the quantitative assessment of the intensity of these infections, not only in the vertebrate but also in the invertebrate host, has been studied in the Liverpool School of Tropical Medicine by workers who believe that such studies not only enable the principles underlying the clinical manifestations to be better understood, but also provide indices which may lead to more precise information on the prospects of control. Elsewhere in this issue Drs. W. E. Kershaw, B. O. L. Duke, and F. H. Budden describe the quantitative assessment of the intensity of infection with *Onchocera volvulus* in the individual and in the community. They show that the numerical distribution of the microfilariae in the skin has a clear pattern which is related to the distribution and severity of the skin lesions and to eye changes and blindness. The understanding of the mechanism of production of this serious complication makes it possible to assess the risk of the development of blindness in any particular individual and therefore to give appropriate treatment as a preventive measure.

Perhaps a more important application of this fundamental principle is in the consideration of transmission of infection in relation to control. Twenty years ago other workers from the Liverpool School of Tropical Medicine drew attention to the fact that in certain insect-borne diseases, in this case malaria, any reduction in the infective density of the vector (although reflected in the age at which the primary attack in children might be expected) was unlikely to cause any obvious improvement in the clinical condition of the adult population until such time as control measures had reduced the infective density of the vector to a figure which no longer caused saturation of the human population with malaria.[2] Dr. Kershaw and his colleagues have shown that a very different state of affairs occurs in the case of the helminth disease onchocerciasis caused by *O. volvulus* and transmitted by biting flies of the genus *Simulium*. The results of these workers' investigations suggest that the introduction of control measures aimed at reducing the infective density of the vector, even if insufficient to lower the incidence

[1] Gordon, R. M., and Griffiths, R. B., in *Modern Trends in Dermatology* (second series), ed. R. M. B. MacKenna, 1954, London, pp. 259–275.
[2] Davey, T. H., and Gordon, R. M., *Ann. trop. Med. Parasit.*, 1933, **27**, 27

of the disease in the human population, might be highly successful in warding off the more serious complications of the disease, and above all might prove successful in reducing the incidence of blindness.

ANGIOMATA

Haemangiomata range from the solitary naevus or "birthmark" to the constituent lesions of a disseminated disease complex, and are of interest from several points of view. They can involve the tissues of many different organs and can assume a large variety of dissimilar forms, with the result that a bewildering array of not very helpful adjectives—such as capillary, tenlangiectatic, cavernous, venous, plexiform, and racemose—are often used to name and describe lesions that are essentially similar. It is unfortunate that no satisfactory account of the whole family of angiomatous conditions exists, although many papers have been devoted to its diverse members.

The solitary naevus is certainly the most frequent type of angioma. It is representative of the bulk of angiomatous lesions in that it is congenital and, as emphasized by Willis,[1] is to be regarded as a malformation rather than a tumour. The clinical development of some of the rare systematized telangiectases makes it clear that vascular tissues retain during postnatal life the capacity for undergoing angiomatous "dysplasia." Thus the lesions of the Osler–Rendu disease, or multiple hereditary telangiectasis (consisting of cutaneous and mucosal angiomata, occasionally with visceral lesions), can appear throughout childhood and even in adult life. These lesions are often on the face, but the condition sometimes becomes evident through haemorrhage from lesions in the oral or nasal mucosa, or from other parts of the alimentary and respiratory tracts. It is unusual among the telangiectases in being hereditary, behaving as a Mendelian dominant in most cases, and is only one of a considerable number of named entities among systematized angiomata, which have been very usefully reviewed by Parkes Weber.[2] They include the Sturge–Weber disease, characterized by lesions of the face and meninges; Lindau's disease, consisting in angiomatosis of the cerebellum and the retina together with certain other developmental anomalies; and the interesting association of multiple cutaneous and soft-tissue angiomata of a limb with accelerated growth of the related long bones, known as the Weber–Klippel syndrome. A recent paper by Shepherd[3] draws attention to the frequency and the surgical importance of involvement of the gastro-intestinal tract, with consequent haematemesis or melaena, in some of these generalized angiomatous syndromes, particularly in the Osler–Rendu type.

Tissues of the skeleto-muscular system are also sometimes affected by angiomata. Angiomata of bone, as described by Bucy and Capp,[4] are most commonly in vertebrae, but also occur in other parts of the skeleton. Angiomata of skeletal muscle, too, are important lesions, although they are not often diagnosed except at exploratory operation. Jenkins and Delaney[5] collected accounts of more than 250 angiomata of muscle reported before 1932, most of them in patients aged under 20 years. Muscles of the lower limb were usually involved, the lesion presenting as a slowly growing mass. A less usual site for angiomata in the deep tissues of the limbs is the tendon sheath. A recent paper by Bate[6] describes three such cases, the tendon sheaths in the hand and forearm being affected. The glomus tumour of Masson,[7] with its clinical syndrome of exquisite sensitivity and trigger pain, is closely related to the ordinary haemangioma; indeed, occasional lesions show a histological structure with features of each of the two conditions.

All the foregoing tumours are benign, if, indeed, they are to be described as tumours at all. Authentic malignant haemangiomas, or "angiosarcomas," such as the metastasizing tumours described by Hall,[8] Wright,[9] and De Nevasquez,[10] are very rare indeed. They are haemorrhagic malignant tumours, occurring in viscera such as the lungs and the spleen, and occasion no confusion with the usual haemangioma. Lymphangiomata are less frequent and less important clinically than haemangiomata, the cystic hygroma being the characteristic lesion of this group. In recent years, however, attention has been directed by Stewart and Treves,[11] in the field of malignant angiomatous lesions, to undoubted lymphangiosarcomata taking origin from the distended lymphatics of the arm in cases of lymphoedema following radical mastectomy operations. A case of this type has recently been reported in Britain by Hall-Smith and Haber.[12]

EXPERIMENTAL PSYCHIATRY

Some drugs administered to cause experimental psychoses are well-known intoxicants that have been used for religious purposes by different people in various parts of the world. Mescaline, harmine, yohimbine, and hashish are some of the naturally occurring alkaloids producing artificial psychoses. Lysergic acid diethylamide (L.S.D.), an ergot derivative effective in minute doses, has been shown by Stoll[1] to act likewise. More recently adrenochrome, an oxidation product of adrenaline, has been found by Hoffer, Osmond, and Smythie[2] to produce similar mental changes. This substance, believed to occur normally in the human body, is the first such to be found which can cause psychotic phenomena comparable to those seen commonly in the acute forms of schizophrenia. The effects of these drugs are most marked on the higher functions of the central nervous system. Visual hallucinations and illusions are common to them all: the sense of time and reality is disturbed, the state of consciousness altered, and a sense of estrangement felt. While with most drugs experimenters are aware that they are under the temporary influence of a drug, volunteers taking adrenochrome lost all insight. Adrenochrome has also been shown to activate latent epileptic activity in the electroencephalogram, and it does this with greater certainty than

[1] *Pathology of Tumours*. London. 1948.
[2] *Rare Diseases*, p. 49. London. 1946.
[3] *Brit. J. Surg.*, 1953, **40**, 409.
[4] *Amer. J. Roentgenol.*, 1930, **23**, 1.
[5] *Surg. Gynec. Obstet.*, 1932, **55**, 464.
[6] *J. Bone Jt Surg.*, 1954, **36A**, 104.
[7] *Bull. Soc. franç. Derm. Syph.*, 1935, **42**, 1174.
[8] *Amer. J. Path.*, 1953, **11**, 343.
[9] Ibid., 1928, **4**, 507.
[10] *J. Path. Bact.*, 1936, **42**, 651.
[11] *Cancer (N.Y.)*, 1938, **1**, 64.
[12] *Proc. roy. Soc. Med.*, 1954, **47**, 174.

leptazol. No comparable electrophysiological changes have been observed with any of the other substances.

Chemically, these substances differ widely, but they have in common an indole nucleus and a substituted amino-ethyl side chain. They thus resemble hydroxytryptamine (serotonin),[3] a pressor substance occurring normally in brain and muscle. Biochemically these drugs—among others—inhibit the enzyme amine oxidase in its detoxicating function of adrenaline, and they also act as antagonists of serotonin. This biochemical and pharmacological action they may owe to their structural relationship, which enables them to compete for receptors of adrenaline and serotonin. Adrenochrome also inhibits hexokinase, and so the oxidation of glucose, by the brain. Nitrogen retention resembling Gjessing's findings in periodic catatonia has been observed during mescaline intoxication.

Here, then, is a group of pharmacologically active substances derived from plant alkaloids and animal sources capable of producing schizophrenia-like states. Woolley and Shaw[4] speculate that serotonin is essential to the maintenance of normal mental function, and that serotonin deficiency may exist in schizophrenia. They suggest that a lack of serotonin or inhibition of its action may cause psychotic phenomena. Any antimetabolite of serotonin, such as L.S.D., could thus give rise to psychotic symptoms. Further experiments are needed to test whether serotonin deficiency really exists either in schizophrenia or in the experimental psychoses. The discovery of the effects of L.S.D. and adrenochrome have thus opened a line of experimental approach to the aetiology of schizophrenia that is supported by some biochemical and pharmacological findings. This in due course could lead to a rational form of treatment. L.S.D. has in the meantime been used in the treatment of neuroses by Sandison, Spencer, and Whitelaw[5] and psychoses by Bush and Johnson.[6] Much larger doses were required in schizophrenics than in normal subjects to produce comparable effects, and it served to accentuate any mood disorder that was present. However, it relieved catatonic symptoms, making the patients more accessible to other forms of treatment. In neurotics they found it helped to relieve severe and long-standing disablement by reviving traumatic memories which were relived during periods of altered consciousness. As such, L.S.D. represents an aid to psychotherapy in the neuroses.

[3] *Schweiz. Arch. Neurol. Psychiat.*, 1947, **60**, 279.
[3] *J. ment. Sci.*, 1954, **100** 29.
[3] See *British Medical Journal*, July 17, p. 144.
[4] Ibid., 1954, **2**, 122.
[5] *J. ment. Sci.*, 1954, **100**, 491.
[6] *Dis. nerv. Syst.*, 1950, **11**, 241.

HORMONES AND SKELETAL GROWTH

For many years clinical observations have made it apparent that the endocrine organs of the body influence general growth, including growth of the skeleton. Obvious examples include the dwarfism resulting from thyroid or pituitary hypofunction, and the skeletal overgrowth resulting from hypersecretion of pituitary growth hormone. As to the development of the skeleton, radiology has made possible the interesting finding that skeletal maturation—that is, the progressive appearance, development, and fusion of secondary centres of ossification—as well as mere increase in size can be affected by hormones influencing growth.

Studies of pituitary dwarfs and cretins show that both the pituitary growth hormone and thyroxine are necessary factors for normal growth. It further appears that androgens, both from the testis and from the adrenal cortex, provide physiological stimuli for the accelerated growth and ultimate maturation of the skeleton at puberty. In contrast, oestrogens, cortisone, and the adrenocorticotrophic hormone of the pituitary have been shown to retard growth—the last presumably by bringing about adrenal secretion of a cortisone-like substance. A recent review by Wilkins[1] summarizes clinical data on skeletal growth and maturation in a wide variety of endocrine disorders.

Although there is no doubt of the reality of these hormonal effects on growth, the interdependence of various endocrine organs makes it very difficult, in both clinical and experimental material, to evaluate the influence of any individual hormone. Thus the removal of the pituitary results in atrophy of the thyroid, while removal of the thyroid results in hypoplasia of the cells of the pituitary responsible for the secretion of growth hormone. Because of this, it has been impossible to interpret with precision many of the experiments designed to determine the specific roles played by the thyroid and pituitary in bringing about normal skeletal growth and development. A recent paper of Evans and his colleagues[2] from the University of California is therefore of considerable interest in that it describes for the first time the results of administration of pituitary growth hormone and thyroxine on skeletal growth and maturation in rats from which both the thyroid and the pituitary had previously been removed. The pituitary was removed by surgical means; the thyroid either by surgery or by treatment with radioactive iodine, which selectively destroys the functioning thyroid tissue. The hormones were administered separately and together and skeletal growth and maturation studied radiographically and by histological study at the end of the experiment. The findings of these workers indicate, as previous work would lead us to expect, that in the rat pituitary growth hormone primarily stimulates skeletal growth and has no effect on maturation, while thyroxine has its main effect in bringing about skeletal maturation, with little effect on growth. There is no doubt that experimental work of this type will continue to throw light on the role of individual hormones in normal growth processes.

[1] *Bull. N.Y. Acad. Med.*, 1953, **29**, 280.
[2] *J. Bone Jt Surg.*, 1954, **36A**, 94.

The Archbishop of Canterbury will dedicate the War Memorial in the Court of Honour at B.M.A. House on November 2 at 3 p.m. Academic dress will be worn for the ceremony. Since accommodation is very limited, early application for admission tickets should be made to the Secretary of the Association, B.M.A. House, Tavistock Square, London, W.C.1.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

L.C.C. OPPOSE SITE IN REGENT'S PARK

London County Council objections to the siting of the proposed new headquarters for the Royal College of Obstetricians and Gynaecologists on Crown land in Regent's Park were the subject of a five-hour Town Planning Inquiry at St. Marylebone Town Hall on September 15. The inquiry was heard before Mr. L. C. WARREN, an inspector of the Ministry of Housing and Local Government. Counsel for the R.C.O.G. was Mr. DAVID WIDDICOMB, and evidence for the College was given by the President, Mr. A. A. GEMMELL, and Mr. LOUIS DE SOISSONS, the architect of the proposed new building. Mr. J. B. CASS and Mr. T. J. CARR represented the L.C.C.

The College's Case

Mr. WIDDICOMB said that the Royal College of Obstetricians and Gynaecologists was endeavouring to carry on its very important work under very cramped conditions at its present headquarters, 58, Queen Anne Street. It was housed in a house which was built as a single family residence many years ago and was given to the College by its first president in 1932. He would particularly draw the attention of the inquiry to the question of the College's museum, which had to be accommodated in one room. One of the College's intentions, when they were able to obtain new headquarters, was to make the museum the finest of its kind in the world.

Last February the site of Sussex Lodge, Regent's Park, came to the attention of the College, and negotiations were begun with the Crown Commissioners to acquire it. Already the Royal Fine Arts Commission, in a letter to the Commissioners, had expressed favourable comment on the proposed design of the College's new building which they considered would harmonize with the fine surroundings. It was proposed to have two entrances to the building, one in Sussex Place, which would be used by Fellows and members, and another in Park Road for goods and staff. Good care would be taken to preserve the many fine trees surrounding the site. There would be 56 examination days a year, and these would be held in the Assembly Hall.

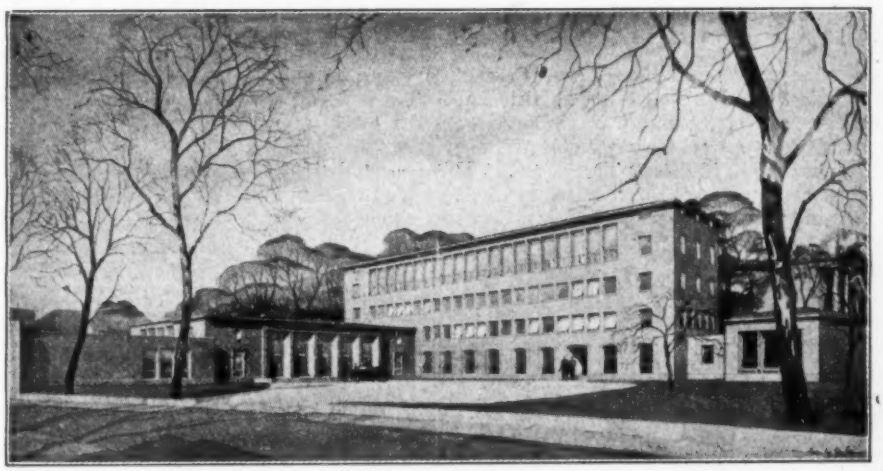
Mr. A. A. GEMMELL, P.R.C.O.G., told the Inquiry that it was not possible to hold written examinations at their present headquarters, and on many occasions they had to hold lectures at the Hall of the Royal Society of Medicine. The College considered that the pathological museum was a major contribution to postgraduate medicine; at the moment it was housed in a small room, and the work of expanding the collection of specimens was severely handicapped. There was no storage space in the present headquarters and the office accommodation was severely limited. The College's journal, which had a world-wide circulation of about 3,000 copies, had to be produced under the greatest difficulties because there was no accommodation for the Editor. The Regent's Park site would be very much more convenient from the standpoint of travel and also because it was on a direct bus route to the library of the Royal Society of Medicine.

Mr. J. B. CASS (for the L.C.C.) said that he did not think that the need for larger accommodation for the headquarters of the Royal College was in doubt, and he had no doubt that Mr. Gemmell would agree with him that that was the position facing many learned institutes. Mr. Cass then raised the question of alternative sites, and suggested that a site in Park Crescent, St. Marylebone, would be even closer to the library of the Royal Society of Medicine.

Flats or the College

The architect of the proposed new College buildings, Mr. LOUIS DE SOISSONS, told the Inquiry that the Royal Fine Arts Commission had already said that the building which stood on the proposed site in Regent's Park, Sussex Lodge, had no special merit and could be pulled down. The new building would have a four-story administrative block which would command fine views over Regent's Park and its lake. He had planned to extend the present Nash wall from Sussex Place.

In his opinion the proposed new College would be preferable on that site to a block of flats; in fact it would be very difficult to produce a block of flats on the site which would harmonize with the Nash buildings in Sussex Place. Furthermore, the nuisance value of a block of flats with 300 or more people coming and going would be very much greater than would be the College with its permanent staff not exceeding 20.



Architect's Drawing of the Proposed New Building for the Royal College of Obstetricians and Gynaecologists.

A site in Portman Place was considered, continued Mr. de Soissons, but it was decided that a building there would look like another block of offices and he did not think that the Royal College should look like that. He had not considered the Park Crescent site proposed by the L.C.C., because he had not anticipated any objection being raised.

Mr. G. SAMES, deputy chief planning officer of the L.C.C., said that he thought the Regent's Park site could support a high-density building such as a block of flats. The county council were satisfied with Mr. de Soissons's design architecturally, but this particular area was primarily a residential area and suitable only for that form of development. The proposed new building could be accommodated on the Park Crescent site suggested already. There the College would be among other professional bodies; indeed, it would be most unfortunate if the College moved away from its associated medical bodies in the area.

Asked by Mr. WIDDICOMB (for the College) whether he would agree that it was easier to design a building such as the proposed College on the Regent's Park site than a block of 102 flats, Mr. SAMES disagreed. He said that any competent architect should be able to design a block of flats to harmonize with the surroundings. In reply to further questions from Counsel, Mr. Sames said that he would not agree that a smaller housing unit on the Regent's Park site would not be an economical proposition.

In his final submissions, Mr. CASS said that whatever was erected in the place of Sussex Lodge it would conform

with the residential development laid down for that area. The great problem these days was to put land to the best possible use, and the county council felt that because of the close proximity to Regent's Park the Sussex Lodge site was ideal for residential development.

Objections by Individuals

Two letters had been received by the L.C.C. from the occupier of No. 20, Sussex Place, which said that he strongly supported the L.C.C. in not allowing the area to be developed other than residentially. Another objector, Mr. S. K. Tubbs, 25, Sussex Place, said that he would not dispute the importance of the R.C.O.G., but to erect the College on the site of Sussex Lodge would be to alter entirely the character of Sussex Place.

Asked by Mr. WIDDICOMB whether he realized that the site would be developed anyhow and would he prefer 102 flats or the College, Mr. TUBBS replied: "I would prefer the flats; at least they would be neighbours and friends and we shouldn't be having sudden avalanches of cars descending upon us."

Concluding Submission for the College

In his final address to the Inquiry, Mr. WIDDICOMB said that the College considered that if 102 flats were built on the site of Sussex Lodge it would be impossible to conform to the building amenities of the area. On the other hand, if many fewer flats than that number were built it could not possibly be an economic proposition. There were therefore some very serious objections to the site's use for residential purposes. In his submission Park Crescent could easily be used for residential purposes.

He had seen the L.C.C.'s plans for the erection of the proposed College buildings on the Park Crescent site, and he did not like them. So far as he could see, the only reason why the L.C.C. wanted to move the R.C.O.G. to Park Crescent was because there were other medical establishments in the area.

In view of the kind of people who would be calling at the College from all parts of the world and from all countries within the Commonwealth he did not think it unreasonable to suggest that the College might be entitled to some special consideration on that account alone.

It was significant also that the Crown Commissioners, who had been most rigid and strict in their tenancy conditions, had not hesitated to negotiate. He was quite sure that if the Crown Commissioners had thought that the Sussex Lodge site had been so eminently suitable for residential development as had been stated by the L.C.C. something would have been done about it before; as it was Sussex Lodge was empty. It was important to notice that all through their negotiations with the Royal College of Obstetricians and Gynaecologists the Crown Commissioners had made it clear that they did not take the matter of choosing an occupant for the Sussex Lodge site lightly.

This concluded the Inquiry, and, in accordance with usual procedure, the Minister's decision will be announced later.

CHILDREN THROUGH THE AGES

Anyone with an hour to spare in the neighbourhood of Harley Street would be well advised to spend it visiting the exhibition on "The Child through the Ages" at 28, Portman Square. This is a two-room exhibition, put on by the curators of the Wellcome Historical Medical Museum from their own treasures, to illustrate the origins and development of the European tradition of child care in its broadest sense.

Starting with the relics of Egypt, Greece, and Ancient Rome, the survey takes us through the Middle Ages to the paediatric practices of the sixteenth, seventeenth, and eighteenth centuries, and ends with the start of the infant welfare movement in England at the close of the last century. Alongside this historical panorama there is a small section illustrating the present-day practices of existing primitive tribes in Africa, North America, and elsewhere. In each period the infant's feeding utensils and cradles, the pictorial records of childbirth and nursing techniques, the magical amulets, and the classical paediatric texts of the times tell their own story. Often it is a terrible tale, as the mortality figures show, and one can only marvel at the resilience of those infants who survived. Fed from pewter bottles impossible to clean, their limbs tightly bound in swaddling-clothes, in the towns often brought up in conditions of unbelievable overcrowding and squalor, with superstition and ignorance the rule among their parents, it is little wonder that so many died.

Only a few of the individual exhibits can be mentioned here: from Ancient Egypt the bas-relief of a cow suckling child and calf together; from modern Egypt the dried fruit to hang round the newborn baby's neck to save it from the jealousy of its brothers and sisters; the cows' horns that were used in the Middle Ages in France as feeding-bottles; the eighteenth-century English nipple-shields, made of silver, to which were sewn heifers' teats, "suitably prepared"; the North-American Indian's papoose-carrier, complete with board to flatten the skull attractively; the necklace of snail-shells to help Jersey babies over their teething; the hollow reed through which the South Angola mother blows an enema into her child—these are some of the bizarre and curious things on view. For the more serious student there is a remarkable collection of early paediatric texts, the cartoons and pictures of domestic life, and the exhibits dealing with three of the great children's hospitals—St. Vincent de Paul's for foundlings in Paris, the Foundling Hospital in London, and the Great Ormond Street Hospital for Sick Children.

The exhibition is open from 10 a.m. to 5 p.m. every weekday (including Saturday), and there is no charge for entry.

SECOND WORLD CONGRESS OF CARDIOLOGY

The combined meeting of the Second World Congress of Cardiology and the 27th Scientific Sessions of the American Heart Association was held last week (September 12–17) in Washington. Dr. PAUL D. WHITE, of Boston, was president of the Congress, which was attended by some 2,000 physicians and scientists from 48 countries, including a strong delegation from Britain. For the first time at a large medical meeting the new international language "Interlingua" (see *Journal*, January 30, p. 283) was used, the abstracts of papers in the official programme being printed in it.

The scientific sessions, comprising symposia, panel discussions, lectures, and papers, went on for five days and covered an immensely varied field. The principal discussions were on cardiovascular epidemiology, with special reference to dietary habits in different countries, atherosclerosis, cardiac surgery, instrumental methods of diagnosis, various aspects of rheumatic fever, the treatment of hypertension, coronary disease, and the rehabilitation of the cardiac patient. During the congress Sir JOHN PARKINSON (London) delivered the Charles Laubry lecture on "Leadership in Cardiology."

It is possible here to report only a few of the many contributions.

Epidemiology of Coronary Thrombosis

The question debated at the opening scientific session was: Why are some populations seriously threatened by heart disease while others are relatively immune? There was general agreement that diet, and especially the amount of fats of all kinds habitually contained in it, seems to bear an important relationship to the prevalence of coronary disease. Dr. GUNNAR BIÖRCK (Sweden) summarized the wartime experi-

ence of the Scandinavian countries, where a forced reduction in dietary fats was shortly followed by a sharp decrease in degenerative heart disease. This was especially true in Norway and Finland, where the change in the diet was greatest. With a return to more luxurious eating after the war, heart disease returned to its former levels. A similar situation was experienced in the Netherlands and in Germany at the end of the war, according to Dr. Biörck, but in the United States, where the fat content of the diet did not fall, no such changes occurred. In England there was a slight decline of dietary fat during the war, and there was a parallel drop in deaths from coronary heart disease among older persons.

Dr. ANCEL KEYS (Minneapolis) pointed out that in coronary disease there was almost always a deposit of cholesterol in the coronary arteries, and that this came from the blood. Experiments in Minnesota indicating that the amount of cholesterol in the blood was related to the total fats in the diet suggested that populations on low-fat diets might be expected to have a low incidence of coronary disease. Research among the Bantu in South Africa, whose diet is very low in fats, tended to bear this out, according to Dr. J. HIGGINSON (Johannesburg). Further support for this thesis came from Professor NOBURO KIMURA (Japan). Investigators from Italy told the Congress that the Neapolitans of southern Italy, who eat much less fat than the Bolognese of northern Italy, suffer less from coronary disease. Blood cholesterol concentrations tended to be higher in Bologna than in Naples, according to recent studies by Drs. Keys and Flaminio Fidanza. Yet the Neapolitans, said Dr. KEYS, were not particularly thin, so, though excessive overweight was harmful, it was not necessary to starve in order to minimize the danger of coronary disease. In England, he said, people tended to be thin, but coronary heart disease was a serious problem.

Dr. J. N. MORRIS (London) emphasized the possible effects of differences in physical activity and "stress." The least coronary artery disease seemed to occur in countries where it was the custom to work hard on a relatively simple, low-fat diet, but there were also some differences between groups in the same country. He had found more coronary disease in England among the upper income groups, especially among doctors, than among those less well off. There was less coronary disease among bus conductors than among bus drivers, and Dr. Morris drew attention to the much greater physical activity of the conductors as a possible cause for this difference.

At a later session it was reported that atherosclerosis could now be induced in monkeys (Harvard University) by giving them a diet low in methionine and cystine, but high in fat and cholesterol. Similar changes had been induced in rats (Buenos Aires). The availability of these susceptible species was expected to facilitate experimental work on the relationship between diet and arterial disease.

Action of Sodium on Heart Muscle

That the low-sodium diet, so often prescribed in cardiac oedema, may also have a directly beneficial influence on the heart muscle was postulated by Professor R. J. S. MCDOWALL (London), who described joint studies with Dr. A. F. Zayat on the utilization of sodium by heart muscle. These studies were based on the knowledge that muscles which are becoming exhausted because of lack of oxygen tend to take up sodium. If the heart's oxygen supply was impaired by disease, reducing the sodium in its environment enabled the muscle to contract more forcibly and do more work. Professor McDowall said that this finding went far to explain why an apparently harmless procedure like taking excessive bicarbonate of soda might be bad for the heart.

Mammary Artery Transplantation for Angina Pectoris

Among the many papers on cardiac surgery was one by Dr. A. VINEBERG (Montreal) describing an operation to improve the blood supply of the heart muscle in cases of angina pectoris by transplanting the internal mammary artery into the left ventricle. After its implantation the mammary artery anastomoses with the coronary circulation. Seven months after implantation, according to Dr. Vineberg, the new circulation had shown itself capable of maintaining function in the left ventricle. It thus provided protection against continued narrowing of the coronary vessels or their sudden closure. More than 90% of these artery implants had been kept open successfully, and he described 28 patients with angina pectoris treated in this way who had been followed for one to four years. The procedure was considered appropriate for patients who were partially or completely disabled by angina but in whom it was not so severe as to produce pain while at rest.

Rheumatic Fever

Since 1934 it has been known that an attack of rheumatic fever is almost always preceded by certain types of streptococcal infection, but the precise nature of the relationship between the two illnesses is uncertain. Dr. A. KELLNER and Dr. T. ROBERTSON (New York) gave a paper which may throw new light on this problem. In 1950 Dr. S. D. Elliott, of the Rockefeller Institute, New York, isolated in crystalline form an enzyme product of the particular strains of streptococci known to be implicated in the infections which precede rheumatic fever. When this crystalline substance, named "streptococcal proteinase," was injected into experimental animals, Drs. Kellner and Robertson found that it caused significant damage to the muscles and valves of the heart, accompanied by an inflammatory reaction. With only a few exceptions, the enzyme's destructive action was confined to the heart. Moreover, when the enzyme was added to the fluid in which an isolated rat heart was beating, contractions soon decreased in strength and frequency, and failure occurred within a few minutes. These findings indicated that streptococcal proteinase is a potent cardiotoxin. It was conceivable that this enzyme and possibly other streptococcal products might play a direct part in some of the cardiac changes that follow streptococcal infections in man.

At one of the sessions on cardiac surgery there was a discussion on whether valve surgery tends to cause a recrudescence of rheumatic fever. Drs. Y. BOUVRAIN, P. FORTIN, and M. CARAMANIAN (Paris) had found ten examples of rheumatic fever recurrences in a group of 120 cases within two months of operation. Dr. A. VERHEUGT (Amsterdam) and his associates had observed rheumatic symptoms in 14 out of 37 patients within six months of operation. Both groups found, however, that there were no serious complications and the condition yielded readily to treatment.

Cardiac Allergy

Dr. J. HARKAVY (New York) thought that in some patients the heart might show an allergic response. Manifestations of cardiac allergy, according to Dr. Harkavy, might vary from disturbances in the rate and rhythm to severe chest pain (as in angina pectoris), or coronary artery disease and damage to heart muscle tissue. Tobacco was the most important irritant or allergen affecting the heart, Dr. Harkavy asserted, but drugs like salicylates and penicillin, pollen, some foods, bacterial infections, and other agents might also produce an allergic reaction. Among other evidence, Dr. Harkavy cited a study of 100 patients with coronary artery disease, all of whom were heavy smokers. He found that 44 had a positive allergic skin reaction to tobacco. They were a relatively young group, averaging 45 years of age. One-third of those who reacted to tobacco had a family and personal background of allergy—a ratio not much smaller than is found in patients suffering from asthma. If noted before serious cardiac damage had occurred, the allergic symptoms were reversible, provided the irritating agent was eliminated or the patient immunized where possible. Similar views on the role of allergy in producing serious disturbances of heart rhythm were also advanced by a group of Argentine physicians, headed by Dr. IGNACIO MALDONADO-ALLENDE.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Detecting Lung Cancer

SIR,—I have read with interest your leading article (*Journal*, September 4, p. 582), "Detecting Lung Cancer." The number of cases of bronchial carcinoma which can be submitted to surgical treatment is slowly increasing, and this appears to be due to the increasing awareness of general practitioners and physicians of the many manifestations of this disease. Any method we can develop to establish the diagnosis at an earlier stage will be most welcome. The emphasis of your leading article was on the cytological investigation of sputum as a diagnostic measure. This undoubtedly takes time and needs a very high degree of skill and experience in the interpretation of the nature of the cells present. The most malignant-looking cells have on occasion been found in cases of bronchiectatic abscess, and there are numerous other pitfalls. It is an interesting confirmatory test, but its use as a primary diagnostic investigation will not receive general agreement. Your comment "For obvious reasons it should precede bronchoscopy" is a very dangerous piece of advice, and if followed valuable time will be lost. You base your advice in part on your statement that "the operation of bronchoscopy with biopsy is rather a formidable business for the patient." This is, of course, true where the investigation is still carried out under local analgesia, but the use of quick-acting relaxants and barbiturates has removed the unpleasantness from this procedure, whilst allowing a more thorough examination of the bronchial tree.

The time and money involved in implementing any policy of routine cytological examination of the sputum appear to be uneconomic, and it is doubtful whether it will bring any more cases to early treatment. For if we make a positive finding and cannot see the carcinoma on *x*-ray examination and cannot see it on bronchoscopy we are no better off from the point of view of treatment by the methods at present available. If it is a peripheral carcinoma, then no difficulty will be had in visualizing it radiologically from a very early stage. If the patient is in the carcinoma age, and bacteriological examination of the sputum shows no leading features, then a small peripheral shadow in the lung which cannot clearly be differentiated from a carcinoma will be treated as such whatever the cytological findings. Fortunately, lobectomy and gland dissection appear to be equally efficacious for this type of bronchial carcinoma as the more radical pneumonectomy, and such treatment is reasonable if the pathological condition turns out to be a chronic inflammatory process. Small growths in the main bronchi will be best diagnosed by bronchoscopy. Growths in the lobar secondary divisions will produce radiological evidence early as tiny areas of collapse. Such growths should be visible by the bronchial telescope or demonstrable as a small block by bronchography. If a positive cytological finding is made, bronchoscopy cannot be escaped if surgical treatment is contemplated. If cytological finding is negative a carcinoma cannot be eliminated and the full investigation programme has to be gone through. If the negative finding is accepted a false feeling of security may ensue until more obvious symptoms or signs develop.

Experience gained from 1,970 patients with bronchial carcinoma at the Liverpool Thoracic Surgical Centre throws into prominence other factors which seem to be much more important in delaying the diagnosis and treatment. Dr. L. Nelson, late medical registrar, undertook an investigation into a consecutive series of 38 cases of bronchial carcinoma admitted to the Centre to find out what factors had been paramount in preventing a patient who has sought advice from his doctor reaching a therapeutic centre earlier.

	Average Days	No Delay	Less than 8 Days	More than 8 Days
Interval between onset of symptoms and first visit to doctor	46·6	5	21	12
Interval between first visit to doctor and *x*-ray of chest	55·8	2	11	25
Interval between first *x*-ray of chest and surgical advice	46·7	0	9	29
Interval between surgical consultation and admission to unit	9·6	3	19	16

From our observations and the above figures the following factors would appear to have some importance. (1) *Patient delay.* It will be seen that 26 out of 38 patients consulted their doctor within eight days, the remainder appearing to be mainly of the type that only seeks advice in the last resort. Such patients are unlikely to respond to any educative propaganda, and on the whole this small series would indicate that "carcinoma propaganda" to the layman would probably be of little value and do more harm than good. (2) *Practitioners' delay.* Increasing awareness and the ability to obtain a chest *x*-ray easily has helped practitioners to diagnose or suspect pulmonary malignant disease much earlier, and with few exceptions further advice is sought with commendable expedition. Although an average figure of eight weeks appears extraordinarily long, under conditions of general practice it must not be considered to indicate any form of neglect, as the earliest symptoms may be so slight and commonplace that the practitioner may have difficulty in suggesting an x-ray or obtaining the patient's consent. Yet here is a stage in the disease in which valuable time is being lost. The answer appears to be the freest facility for *x*-rays to the practitioner, as at this stage clinical signs are of little value. It is customary to combine an *x*-ray with a consultation with a chest or general physician at clinic or hospital, but if this involves an appointment system then the patient with a carcinoma is jeopardized. It would seem advisable that some priority arrangement for cases of suspected carcinoma should be established and brought to the notice of the general practitioners. (3) *Radiologists' delay.* It is still the practice of a few radiologists, no doubt from a natural pride in their work, to attempt to make an accurate radiological diagnosis of the condition within the chest by suggesting serial radiographs. This is not in the patient's best interest, and it is now generally recognized that, while there may be very good grounds for strongly suspecting a carcinoma, it is frequently impossible to be sure radiographically whether a shadow is simple inflammatory, tuberculous, or neoplastic. We suggest that in any report sent outside a hospital or radiological centre describing an abnormal shadow the phrase "further clinical investigation is required" should be routinely used. (4) *Delay in admission to the ward from chest clinic or out-patient department.* The difficulties of this stage are fully recognized, particularly where out-patient departments and waiting-lists are large. Few cases of bronchial carcinoma should, however, require any prolonged admission to the general wards for the diagnosis to be established. *X*-ray, sputum examination, and bronchoscopy can all be undertaken as out-patient investigations or at the most after admission to hospital for 24 hours. One would emphasize once again that the diagnosis of an early bronchial carcinoma frequently requires bronchoscopy by a team highly experienced in this disease.

Much time can be saved by accepting the fact that a patient with a suspected bronchial carcinoma has an emergency condition, and that the organization for the treatment of surgical emergencies should be adopted. I would maintain, Sir, that if the diagnosis of bronchial carcinoma is to be made earlier it would be more profitable to direct efforts to obviate the delays that I have enumerated above rather than to establish an expensive personnel to look for malignant cells in sputum.—I am, etc.,

Liverpool, 1. F. RONALD EDWARDS.

Smoking and Lung Cancer

SIR,—Surgeon Captain T. L. Cleave (*Journal*, September 11, p. 645) refers to my letter (*Journal*, July 31, p. 303) dealing with the relationship between smoking and cancer. He quotes my statement: "The distribution of cancer is constantly shifting from one organ to another, but the total incidence of cancers remains about equal." Substituting

his own conclusions for those I made from the above statement, he writes: "Dr. Blond therefore argues that to escape from the Scylla of cancer of the lungs is but to fall into the Charybdis of cancer, shall we say, of the stomach." He then goes on to argue against his own conclusions by saying: "But the more cancers we avoided, the longer we should live." I wonder how many cancers Surgeon Captain Cleave has avoided in the past.

Surgeon Captain Cleave does not discuss the relationship between smoking and cancer. Instead, he invents fictitious cases amongst aniline-dye workers, one of whom, he tells us, avoids cancer of the bladder by changing his occupation at the age of 40, is cured of cancer of the colon by means of surgery at 60, and survives to the ripe old age of 100 before he finally succumbs to cancer of the throat. Surgeon Captain Cleave is evidently an optimist, for in claiming the prolongation of life for 40 years by means of surgery he ignores the fact that more than 95% of cancer victims of the stomach, colon, and all the other internal organs are irrevocably dead in less than five years, in spite of surgical treatment. As to the question of a man avoiding cancer of the bladder by changing his occupation, a study of the statistics is revealing. Although the annual total mortality rate from cancer among all sections of the community remains more or less constant, it is true that 71.4 per 100,000 workers exposed to aniline dyes develop cancer of the bladder, whereas the annual incidence of cancer of the bladder among the population as a whole is only 2.1 per 100,000. Nevertheless, only 0.07% of aniline-dye workers develop cancer of the bladder while 99.93% do not. I should be interested to know on what grounds Surgeon Captain Cleave chooses to assume that his hypothetical case belongs to the minority group of 0.07% of aniline-dye workers that will develop cancer of the bladder and not to the majority of 99.93% who will escape it.

What protects this 99.93%? Why do the majority of aniline-dye workers escape cancer of the bladder, just as the majority of smokers escape cancer of the lung? Does this not confirm my view that the so-called carcinogenic toxins have only the effect of shifting the site of cancer from one organ to another? For further instances providing evidence for my statement, I would refer Surgeon Captain Cleave to my book, *The Liver and Cancer: A New Cancer Theory*.[1] —I am, etc.,

London, W.1. K. BLOND.

REFERENCE

[1] *The Liver and Cancer*, 1954. Wright and Son, Bristol.

Pancreatic Carcinoma

SIR,—Professor Charles Rob and Mr. Rodney Smith's article (*Journal*, August 7, p. 330) on the diagnosis of pancreatic carcinoma should encourage and challenge our diagnostic acumen. Dr. R. D. Lawrence's letter (*Journal*, September 4, p. 593) was of great interest in drawing attention to the presence of diabetes as the first sign in twelve of his cases. It is probable that similar cases have been seen but not recorded. Professor Allen O. Whiffle[1] states that there may be glycosuria, but this is rare. One of my patients, a lady aged 63, had had intermittent glycosuria, without signs or symptoms of diabetes, for three years before cancer of the pancreas produced hepatic metastases.

In general practice I find that regular weighing of patients and occasional urinalysis can be of great help in assessing cases of "cancer age." Asthenia, anorexia, and loss of weight are ominous symptoms. The characteristic boring or grinding type of pain extending through to the back is a commoner early symptom than painless jaundice with a palpably enlarged gall-bladder.

It is possible that the growth can be present for months, or even years, without causing any suspicious symptoms.—I am, etc.,

Morden. G. LEWIS JONES.

REFERENCE

[1] In *A Textbook of Medicine*, 1943, edited by R. L. Cecil and F. Kennedy, 6th ed., p. 796. Saunders, Philadelphia.

ABO Blood Groups and Toxaemia of Pregnancy

SIR,—Drs. L. A. Pike and A. M. Dickins in an important contribution (*Journal*, August 7, p. 321) have produced evidence to indicate the marked preponderance of the blood group O in their toxaemic patients amongst whom heterotopic foetuses tend to predominate. They have suggested that a variety of antigen–antibody reaction arises as a result and produces a humoral pressor substance that damages the smaller maternal vessels, provoking, among other effects, oedema, albuminuria, and severe anti-diuresis. Regarding the causation of generalized oedema much research has confirmed that abnormal capillary permeability is not its basis. Accurate measurements of the protein in oedema fluid give it a range from 0.10 to 0.48 g.%, a concentration insufficient to overcome the osmotic pressure of the plasma proteins and to attract fluid out of the vessel wall.[1–4] Neither, therefore, can oliguria be explained by such fluid loss into the tissues as a result of vascular damage. Albuminuria has recently been held to be due to the failure of reabsorption of albumen now claimed to be a normal constituent of the glomerular filtrate. Be that as it may, the researches of Bradley[5] have shown that in acute nephritis the erect posture still further reduces the glomerular filtration rate and is accompanied by a correspondingly increased albuminuria confirming that protein leakage is the result of particular ischaemic damage to the glomerular capillaries.

Humoral substance is undoubtedly responsible for the toxaemic hypertension. Experimental and therapeutic evidence indicates that the ischaemic kidney produces such pressor material. The normal kidney, on the other hand, can effect its destruction.[6–24]

Experiments with hexamethonium which the authors quote have not been shown to overcome renal ischaemia as far as I know, possibly because of the size of dose, and fail in consequence to ameliorate the toxaemic state. They do not exclude the renal origin of the pressor material, but, when viewed against the background of the evidence to follow, emphasize it. For the pre-eclamptic symptomatology, including the hypertensive state, is greatly improved when renal resistance has been overcome by therapeutic measures, that comprise "renal denervation" by caudal anaesthesia reaching the 10–11 D. segment[7–11] and the experimental or therapeutic exhibition of "veratrone," dihydroergocornine, hydrallazine, and rauwolfia,[12–18] which help to overcome renal resistance. The vasculotoxic effects observed in brain and kidney could be explained as intrinsic in renin action, since these lesions can be produced by angiotonin in rats treated with deoxycortone and salt.[19]

Incontrovertible proof that the vasculotoxic processes in the brain arise as a sequel of renal ischaemia when the hypertension is excessive has just recently been furnished by Byrom.[20] He has shown that encephalopathy ensues as a result of hypertensive changes initiated in rats by application of the Goldblatt clamp and that "spasm of the cerebral arteries and focal oedema are closely correlated with acute cerebral symptoms. Arterial necrosis though often present is not essential to the causation of these symptoms." The removal of the clamp immediately and dramatically abolishes encephalopathy and tends rapidly to reduce the blood pressure to normal, confirming that renal ischaemia is the basis of toxaemia. Post-partum eclampsia is explicable on an existing theory. Franklin[21] has shown that griping movements of the puerperal uterus in the rabbit evoke renal ischaemia. The application of this finding, which is in keeping with the thesis that the utero-renal reflex is the basic aetiological factor in eclampsia, offers an explanation for the occurrence of post-partum eclampsia or of mounting hypertension in the puerperium. Unless the antigen–antibody reaction envisaged is shown to be responsible for the renal ischaemic change its importance in the aetiology must be secondary. However, Platt[22] has suggested that the onset of acute nephritis on the fourteenth day after tonsillar infection could be ascribed to an allergy. But on the other hand staphylococcal toxin has been shown by de Navasquez[23] to

produce renal changes of an ischaemic order, and this fact could equally be advanced as the causative factor of the nephritic condition.

In the present stage of our knowledge a satisfactory integration of Drs. Pike and Dickins's findings does not appear possible. But in the striking incidence of group O individuals amongst those suffering from toxaemia it behoves us to continue our search for the aetiological significance of this association.—I am, etc.,

London, W.1. JOHN SOPHIAN.

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Blood Groups in Relation to Certain Diseases

SIR,—In reference to the excellent article by Aird *et al.* (*Journal*, August 7, p. 315), and as one who contributed to earlier literature on the subject of the blood groups in relationship to certain diseases,[1] it is probable that the error of "inaccuracy of diagnosis" is not too great when it is remembered that the series of cases of the blood diseases grouped were diagnosed by such eminent haematologists as Drs. J. F. Wilkinson and M. C. G. Israels, and the cerebral neoplasms by such a distinguished neurosurgeon as Sir Geoffrey Jefferson. Also, it will be noted, in my article considerable caution in interpreting any "findings" is advised in very similar terms to that advised by Professor Aird. Nevertheless, taking the category of pernicious anaemia, let the figures speak for themselves. As compared with the general hospital population there would appear to be an unusual incidence of B and AB :

	No. of Cases	O	A	B	AB
Pernicious anaemia	193	80 (41·45%)	75 (38·9%)	25 (12·95%)	13 (6·7%)
Hospital population	1,927	939 (48·72%)	792 (41·1%)	148 (7·68%)	48 (2·49%)

When this article was published the science of statistics as now so generally applied in medicine was not then so generally applied. If some statistical expert finds the series in my article is not too small, let him apply this yardstick to bear out or cancel out any question of an unusual incidence. At the time, as I remember, I noted in my article that some of the severest cases of blood disease grouped fell into the B–AB categories. Whether this is by chance or not is, of course, anyone's guess.—I am, etc.,

Ayer, Massachusetts. KENNETH I. E. MACLEOD.

REFERENCE

1 *British Medical Journal*, 1937, **2**, 745.

Torsion of Normal Fallopian Tube

SIR,—According to Professor Lambert Rogers's letter (*Journal*, August 13, 1949, p. 384) there were 21 or 22 cases of torsion of normal Fallopian tubes reported in the literature up to that time. We had the opportunity to have under our care recently two similar cases, and because of the rarity of this condition we would like to report these two cases and three others which are to be found in the Greek literature.

Professor Kontiadis[1] reported two cases in 1931 and B. Kourias[2] another in 1939. Our two cases are as follows. (1) Woman of 30, married. The first symptoms of the torsion appeared on the day of her menstrual period. She was examined fourteen days later and a palpable Fallopian mass was found. The diagnosis was made pre-operatively and was confirmed at operation. (2) Woman of 33, married. The symptoms appeared the day before the first day of the menstrual period. She was operated on as an abdominal emergency. In both cases we performed salpingectomy, because the tubes did not appear to be viable. However, we believe that in cases with uninjured tubes, when restoration of the torsion and the maintenance of the Fallopian tube is possible, it is necessary to attach it as it fits so as to avoid any relapse. In cases with long infantile mesosalpinx, its shortening is advisable.—We are, etc.,

D. MAYIAKOS.
Athens. ALEX ROMANOS.

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Chlorpromazine in Psychiatry

SIR,—I read with interest the papers on the use of chlorpromazine which appeared in the recent issue of your *Journal* (September 4). In my opinion, it is too early to conclude whether a symptom only or a whole psychiatric syndrome will be found to respond to chlorpromazine. It seems certain, however, even from the limited material published until now, that we have acquired a new powerful drug for overcoming tension and agitation. I had cases with catatonic excitement which, as is well known, always presented psychiatrists with great difficulties as regards sedation. We have to use large doses of barbiturates, and often the patient becomes more disturbed than ever. I used chlorpromazine and the patients became rapidly manageable. In one case on the fourth day of 200 mg. of chlorpromazine per day the patient was free from hallucinations.

I found in quite a number of my cases receiving up to 200 mg. of chlorpromazine daily an increased sedimentation rate : in one case the E.S.R. reading was 50 mm. in the first hour without accompanying rise of temperature. I wonder whether this fact could be taken as a possible line of research into the mode of action of chlorpromazine. I think that it is worth pursuing in order to elucidate the true mechanism of chlorpromazine, about which very little is known at present.—I am, etc.,

Tonbridge. G. BRAM.

Chlorpromazine and Jaundice

SIR,—The recent reports of jaundice occurring during the administration of chlorpromazine require clarification. Dr. R. H. Boardman, in his report of a fatal case (*Journal*, September 4, p. 579), states that throughout the 13 weeks' course of the jaundice the patient's stools were pale or near-white and the urine was heavily laden with bilirubin. The serum bilirubin and alkaline phosphatase were grossly elevated, while the serum proteins, thymol turbidity, and colloidal gold remained normal. In addition, the patient had pruritus. These clinical and biochemical features are generally regarded as being characteristic of obstructive jaundice. The necropsy report states that microscopic examination of the liver supported a diagnosis of "toxic hepatitis," and no mention is made of obstruction of bile ducts or canaliculi. In one patient mentioned by Professor J. Elkes and Dr. Charmian Elkes (*Journal*, September 4, p. 560) jaundice occurred shortly after a course of chlorpromazine. Clinical details are not given, but the serum bilirubin was raised while the tests of hepatic cellular function remained normal. This picture again is consistent with an obstructive type of lesion. Drs. Gerald Garmany, Anthony R. May, and Aleck Folkson in their recent paper (*Journal*, August 21, p. 439) refer to three patients who excreted bile salts in their urine and who showed abnormal

bromsulphthalein retention, but in these cases the serum bilirubin remained normal. Three of the 71 patients treated by Lehmann and Hanrahan[1] developed jaundice "with the attendant blood and urine abnormalities," and in these patients the cephalin–cholesterol flocculation test was abnormal. These authors found minor abnormalities in the cephalin–cholesterol flocculation test in one-half of their series of patients receiving chlorpromazine, although jaundice was observed in only three cases. If, in these reported cases, jaundice was in fact attributable to the action of chlorpromazine then the published clinical and biochemical findings show considerable variation. A plea is made for more detailed study of these cases, including liver biopsy, so that the mechanism of this important complication of chlorpromazine therapy may be elucidated.—We are, etc.,

J. G. MACARTHUR.
Glasgow, W.2. BERNARD ISAACS.

REFERENCE

[1] *Arch. Neurol. Psychiat. (Chicago)*, 1954, 71, 227.

Selection of Medical Students

SIR,—Dr. F. Gugenheim (*Journal*, September 11, p. 647) is quite wrong. The very last thing any reasonable man wants is a mass standardized student; for if the standard chosen is wrong, every student in the university will be unsuitable. Let Mary's choose brawn, U.C.H. brain, and let Bart's continue to let in what she deems to be gentlemen. The result will be the British doctor, which I am sure Dr. Gugenheim will agree is the best that privilege can buy.—I am, etc.,

Ipswich. JOHN STEVENS.

SIR,—It was with considerable interest that I read Dr. Maurice Davidson's letter (*Journal*, September 4, p. 594) on the "Selection of Medical Students," following as it did upon Dr. D. Brinton's earnest article (*Journal*, August 28, p. 483). Perhaps these eminent gentlemen, and others, would be interested to know how much many of us recent graduates regret the lack of a grounding in the humanities. It was my own experience to enter medical college straight from school, where latterly the educational bias was, perforce, upon scientific subjects. At college I found myself in fierce competition with newly returned war service men who undoubtedly, as Dr. Brinton observed, set a very high standard. Now, however, when I am in the company of friends who pursued more intellectual paths at university, I am well aware of my insufficiency in their conversation. Only since embarking upon my National Service does there seem to have been the time to indulge in the more gracious pursuits of literature, music, and art. I know I am not alone in this cultural poverty.

What, then, is the answer? To add two or three more years to the already lengthy period encompassed by training, pre-registration, and National Service would mean that a man might well be 30 before he could at last embark upon his chosen career. But how much better fitted would he be to take his place as an intelligent member of society. It would be of interest to learn the views of your readers on this vexed problem.—I am, etc.,

B.A.O.R., 8. WILLIAM M. WILSON.

Why be a Doctor?

SIR,—Of course the great majority of those who take up medicine want to be good doctors. Equally, we expect that hard work when we are young will earn us a fair chance (we have never asked for guarantees) of being able as we grow older to continue working in our chosen field at a reasonable income. The suspicion that this chance is being denied will degrade our work from a service to others down to a cut-throat competition amongst ourselves. At a time when everyone is talking about a surplus of doctors, the medical schools are maintaining their present high intake, or even in some instances increasing it. Why?—I am, etc.,

London, W.1. P. MESTITZ.

The Work of a Ship Surgeon

SIR,—Dr. G. L. Alexander's letter (*Journal*, September 4, p. 594) is a timely reminder that the life of a ship surgeon can be a full one, rewarding in the wide range of clinical experience offered and in the changing population which comes under his care. He has referred to the fact that this branch of the profession is little known. It was interesting to note that it was not even referred to in the annual educational edition of the *Journal* (August 28) although many other fields of medicine were brought to the notice of the young practitioner.

A large ship is a small town in itself and the community on her will provide examples of all the types of patient to be met with in general practice—and more. Not only will the ship surgeon be called on to deal with the many aspects of disease that his shoreside brothers will, but also with a broad spectrum of mankind from all corners of the world. The doctor thinking of going to sea need not fear that his talents will be wasted, nor that he will lack in clinical material. His work will include the normal run of less dramatic cases, of course, but he will also be called on to deal with accident casualties, the management of epidemics in a closed community, and acute medical and surgical emergencies. His role will be manifold. The "surgeon" is public health officer, physician, casualty officer, paediatrician, psychiatrist, and dentist. He will also be clinical pathologist (and sometimes morbid pathologist and radiologist: most big ships have facilities for minor laboratory procedures and *x*-ray apparatus). Thus, the responsibilities are many and varied, but medicine can be practised to the fullest extent that the ship surgeon wishes. Life at sea is an interesting one and a full one. As Dr. Alexander pointed out, it is not one for escapees. It has its drawbacks as well as its rewards, but the rewards outweigh the drawbacks.—I am, etc.,

Fowey, Cornwall. D. HOLMAN MATTHEWS.

Treatment of Status Asthmaticus with Nitrogen Mustard

SIR,—Dr. D. D. Vora (*Journal*, July 24, p. 242) has raised two points regarding the data presented in my case report on "Treatment of Status Asthmaticus with Nitrogen Mustard" (*Journal*, June 26, p. 1475). Regarding the first point, I would like to state that the white blood cell count was done by the late Brigadier R. P. Cormack, of the Laboratory of Clinical Medicine, Nairobi. I referred the question to Dr. A. Henderson-Begg, his colleague at that time and the present director of the same laboratory, who comments as follows:

"The point that Dr. Vora raised about the white cell count is rather a peculiar one, and does not appear to have any bearing on your case one way or another. I suppose what is worrying him is the fact that the figures suggest a degree of accuracy that our present methods are incapable of attaining. He is quite right, but it should not be very difficult for him to correct the figures to the nearest 50 or 100 or even 200, whichever he prefers. The count was done by the late Brigadier R. P. Cormack, a very experienced pathologist, and he always reported them like this—a personal idiosyncrasy if you like—relying on the intelligence of the doctor to whom the report was made. All bulb pipette methods of counting blood cells are highly inaccurate (especially red cells) and we have recently discarded these methods altogether. I think, however, that you can safely assure your correspondent that the figures given are accurate within the generally recognized limitations of the method."

As to the second point raised by Dr. Vora, that at the commencement of treatment I stated that vomiting might help the patient by liquefying the tenacious secretions, and that in the second and further treatments an attempt was made to prevent the vomiting by giving phenobarbitone, it appears that Dr. Vora did not read the case report carefully. The answer appears to be fairly obvious. The first injection of nitrogen mustard was given when the patient was in an acute asthmatic state. It was considered that liquefaction of the tenacious bronchial secretions was desirable at this stage, and hence no attempt was made to prevent the vomiting. A few hours after the injection the tenacious

bronchial secretions were greatly liquefied and the patient was able to expectorate with great ease. The vomiting had served its desirable and useful purpose. Any further vomiting was undesirable, and hence attempts were made at this stage to control it. The second and subsequent treatments were given when the patient was free of asthmatic symptoms. The bronchial secretions were already loose and expectoration was easy. Vomiting would have served no useful purpose at this stage and was an undesirable side-effect of nitrogen mustard, and hence attempts were made to minimize it during the second and subsequent treatments.—I am, etc.,

Nairobi. B. P. ARYA.

Side-reactions to Benethamine Penicillin

SIR,—Drs. M. G. Nelson, J. M. Talbot, and T. B. Binns (*Journal*, August 7, p. 339) report the occurrence of a hard tender lump in the buttock in 4 out of 120 patients receiving the above injection. So far in general practice I have given about 200 injections of benethamine penicillin, and have had the unfortunate experience of causing 15 patients to develop similar hard, very painful lumps which have taken up to two weeks to disappear. These patients were not keen to have further injections of benethamine. In some cases it was only the second or third injection that caused the reaction.

I have not found benethamine useful for initiating treatment of the common illnesses in which penicillin is indicated, but once treatment had been started with sodium or procaine penicillin, and a satisfactory clinical response obtained, then benethamine could be substituted with success at 48-hour intervals in doses of 300,000 units in adults and children.—I am, etc.,

Goodwood, S. Africa. G. J. BUDOW.

Danger from Methyl Chloride

SIR,—Having recently read the article "A Case of Methyl Chloride Poisoning," by Dr. M. M. Macrae (*Journal*, May 15, p. 1134), I am prompted to put on record a case illustrating the explosiveness of this gas.

In April an explosion occurred in the bar of a hotel in Cunnamulla (Western Queensland, Australia) resulting in the death of seven of the men in the room and the total destruction of the hotel by fire. A coroner's inquiry has assessed the cause of the disaster to be the ignition of an explosive mixture of methyl chloride (from a faulty refrigeration system) with air by a match being used to light a cigarette.—I am, etc.,

Goomeri, Queensland. R. G. SCHULZE.

Crooked Thinking in Medicine

SIR,—I should like to welcome and to support Dr. Richard Asher's plea (*Journal*, August 21, p. 460) for a better understanding of the crooked ways of thought in Medicine. To seek out crooked thinking, as Dr. Asher suggests, is a useful exercise for the practitioner; whether he can avoid it is another matter. It may be enough if he recognizes it and is not taken in by words and the human propensity to hypostatize them. Not only in the field of psychiatry, but in every field of natural science, we have the same trouble with words—that if there is a word for a particular thing, we become convinced that such a thing exists. The reason for this is that we do not distinguish clearly, with Kant; between regulative and constitutive principles, and are apt to accept as an established fact what merely is a scientific hypothesis or abstraction. (The controversy on evolution is the best example.)

The public will call a rhinitis a cold, thus making a cause into a nosological entity, a thing which can be caught and thrown off; they will call a myalgia rheumatism, imagining this to be a "thing" which shifts about in the body. They always want to know what "it" is and are not satisfied until we have put a name to the symptom. They are even convinced that the invisible entity of disease can be made visible by *x* rays. I think a doctor has to make allowances for this, though he need not be deceived himself. He has to be particularly patient with views on causation. If a cancer specialist tries to persuade him that the cause of cancer is a microbe or a virus, he has no means of straightening his crooked thoughts; but when a patient with a boil asks him, "What do you think is the cause of it? I never had it before," he is in a real dilemma. Is there an answer to this question which satisfies the patient, the doctor, and formal logic?—I am, etc.,

London, N.W.1. F. M. LEHMANN.

Routine Distribution of Vitamins

SIR,—The 1953–4 report of the Committee of Public Accounts reveals an expected loss of £650,000 on concentrated orange juice. Is it not time that the medical profession raised a protest against the routine distribution of vitamin preparations? The provision of vitamin supplements was a wartime expedient to offset the shortage of fresh fruit and the rationing of fats. Now that oranges are obtainable all the year round and butter and vitaminized margarine are freely available I see no reason for continuing the supply of concentrated orange juice and cod-liver oil to all children under 5 years of age and vitamin capsules and orange juice to all expectant mothers.

As far as calcium and vitamin D are concerned it is difficult to understand how even a careless mother could deprive herself or her family. The expectant mother receives one pint of cheap milk a day. The bottle-fed baby has a choice of dried milks which all contain about 300 i.u. of vitamin D per oz. (28 g.). Proprietary weaning foods all contain added calcium and vitamin D, one of the most popular containing as much as 1,000 i.u. of vitamin D per oz. All brands of margarine contain 80–100 i.u. of vitamin D per oz. and all flour, except 100% wholemeal, has 0.003% of added chalk. What justification is there for reinforcing these very adequate antirachitic defences by the distribution of vitamin A and D tablets to all expectant and nursing mothers and cod-liver oil to all children under 5?

With regard to vitamin C the position is different. The mother who chooses an ill-balanced diet or cooks badly may deprive her family of this vitamin. But it is a reasonable assumption that the mothers who are indifferent about dietary vitamin C are among the many who do not trouble to fetch their orange juice from a distribution centre. Babies fed too long on dried or boiled milk are the only people likely to suffer from clinical vitamin C deficiency. Could not their mothers be persuaded to spend eightpence of their eight shillings family allowance to buy two oranges a week which would supply all the necessary vitamin?

The welfare service is not alone in its indiscriminate dispensing of vitamins. In hospitals the routine administration of vitamins to ward patients is a common practice. If this is justified on the grounds of faulty diet then the remedy lies in the hands of the management committees. However, the quantity of vitamins given often suggests an assumption that vitamins act as a tonic. But, as Dr. Richard Asher has recently pointed out in your columns (*Journal*, August 21, p. 460), it is crooked thinking to argue that because a vitamin makes good a deficiency it therefore makes better someone without a deficiency. Last year I investigated the consumption of "routine vitamins" at a 250-bedded hospital. The average dose was 7 tablets, capsules, etc., a day for each patient. On one ward each patient was given 18 tablets a day, thereby receiving more than ten times the normal requirement of vitamins A, C, and D. The total cost of these unprescribed vitamins in this hospital in 1952 amounted to £300.

The remedy for all this waste of public money is simple. Let the preventive medicine of the welfare service educate the public on the value of protective foods and, where necessary, fortify inadequate foods. But let it stop supplying us with routine additions which should have been made redundant for the majority. Let the general practitioner and hospital services take over where the public health services leave off. Those people who, by reason of disease,

debility, surgical operation, or other special requirements need extra vitamins should obtain them on prescription, and only as long as the need exists.—I am, etc.,

Bridgend, Glam. A. W. FOWLER.

Ring Incorporated in Finger

SIR,—Dr. I. J. Macqueen's ingenious method of overcoming this trouble (*Journal*, August 21, p. 471) is more difficult than the following method, which, incidentally, I found most effective in paraphimosis. Soak gauze in a solution of 10% cocaine and 1 in 1,000 liquor adrenalin.; apply to the oedematous part of the finger; apply a bandage; leave on for 10 to 15 minutes. The ring can now be manipulated easily over the finger, which has lost most of its oedema.—I am, etc.,

Beckenham. A. J. AMBROSE.

Are Accidents Inevitable?

SIR,—To the most interesting hypothesis in your leading article (*Journal*, August 21, p. 455), explaining the self-limited proclivity to accidents of the group of young accident-prone miners, the hypothesis of adaptation could be added. On theoretical and on practical grounds the assumption can be made (according to Bell, Davidson, and Scarborough[1]) that the defence reflex is conditioned, like most if not all reflex activities. The reflex continues at full strength or enhanced after a great number of repetitions if it is followed every few times by reinforcement. The strengthened defence reflex produces adaptation.

The practical sequel for this hypothesis is given in the Report of the Industrial Fatigue Research Board of 1920.[2] The adaptation period required to improve the hourly output (in metal workers) after reduction of hours of work was found to be longer in the more complex operations than in the simpler work. The time factor also enables the young accident-prone miner to improve his perceptual acuity, to develop his cognitive functions, and to learn the evaluation and prevention of hazardous situations. *Tempora mutantur et nos mutamur in illis.*—I am, etc.,

Cardiff. ALFRED BECK.

REFERENCES

1. *Textbook of Physiology and Biochemistry*, 1950. Livingstone, Edinburgh.
2. Medical Research Council, *Report of Industrial Fatigue Research Board*. London, 1920, No. 6.

Incomplete Rupture of Pectoralis Major

SIR,—I was most interested to read Mr. W. B. Law's case of incomplete rupture of the pectoralis major (*Journal*, August 28, p. 499). I described a similar case in the *Journal* of November 8, 1941 (p. 652), and although the two cases are not exactly similar (in my case the arm was struck a glancing blow whilst in the position of abduction and external rotation), here too the diagnosis was not made for nearly a month after the accident, the initial *x*-ray being negative when the patient attended the casualty department. No active treatment was advised, and full movements were regained. It would appear that, even if the diagnosis is made immediately, conservative treatment is all that is required.—I am, etc.,

Barnsley, Yorks. A. G. BUTTERS.

A Mysterious Pain

SIR,—We should like to report a case of apparent labour pains occurring in a young boy.

A woman aged 27, 40 weeks pregnant, was out walking with her two children when the elder child, aged 2 years 11 months, burst into tears, complaining of pain and pointing at his throat. He cried for about a minute and then appeared to return to normal, saying that the pain had gone. One minute later his mother experienced her first labour pain. A repetition of the whole cycle occurred a few minutes later and was repeated at regular intervals for over three hours, as long as the mother remained with the child. After she had put him to bed and left him, he showed no further signs of being in pain, and soon went to sleep, whereas his mother's labour continued in another room for a further four hours. We were present throughout these events. We checked the intervals between the pains with a watch. At first the mother's pains occurred every ten minutes, and after three hours were occurring every four to five minutes. On every occasion the child's pain preceded the mother's by two minutes and lasted the same length of time. He cried on every occasion. The mother showed no outward signs of pain and made no reference to it in front of the child. We questioned the child about his pains. Sometimes he pointed at his throat, but mostly he was vague, merely indicating his inside. On examination of the child no abnormality was found. The next morning he appeared to have no recollection of what had taken place. The boy had not been present during his mother's previous labour. The younger child, a boy aged 18 months, behaved in a normal fashion throughout.

It is difficult to interpret this case by any recognized psychological or physiological theories. Possibly it is a case of extra-sensory perception, or perhaps just coincidence. We should be very interested to know whether anyone else has had or has heard of similar experiences, or can offer an explanation of them.—We are, etc.,

P. J. DALLY.
London, S.W.9. A. G. MULLINS.

Window-cleaner's Finger

SIR,—The photograph illustrates a deformity of the index fingers which I have not seen recorded. I venture to call it window-cleaner's finger. The patient was a man of 60 who had been a window-cleaner for 25 years. He was admitted to my care at the Leeds General Infirmary for

an unconnected condition. The terminal joints of both index fingers showed a permanent radial deviation. The deformity was more marked on the right index finger.

I was informed by my patient that to clean a window fully one should finish by wrapping the duster or leather round the index finger and run it along the glass where this joins the window frame. Constant repetition of this action had produced the deformity.—I am, etc.,

Leeds P. J. MOIR.

Cure for Baldness

SIR,—Many members of the profession will be aware that, following Dr. John Kelvin's interesting note (*Journal*, September 11, p. 648) reporting the appearance of new hair growth in two patients being treated with β-pyridyl carbinol ("ronicol") for peripheral vascular disease, the subject has received considerable publicity in the lay press. As we, and no doubt many doctors also, have been pressed for further information we take this opportunity of stating that at present we know no more about the subject than appeared in Dr. Kelvin's communication. To the best of our knowledge the effect he observed has not been previously reported, and we must therefore await the results of controlled clinical investigations before forming an opinion as to whether this drug could be generally recommended as a treatment for baldness.—I am, etc.,

London, W.1. MARGARET BRIGGS,
Medical Adviser to Roche Products, Ltd.

Obituary

ALFRED COX, O.B.E., M.A., LL.D., M.B.

A memorial service for Dr. Alfred Cox, former Medical Secretary of the British Medical Association, was held at St. Pancras parish church on September 16. The congregation included many members of the Association Council, past and present; two former Chairmen of Council, Sir Henry Sessions Souttar and Dr. H. Guy Dain, and the present Chairman, Dr. E. A. Gregg; the principal officials and many members of the Headquarters staff; representatives of various public bodies and societies; and many personal friends. The General Medical Services Committee, which was meeting on that day, adjourned to permit its members, headed by their chairman, Dr. Talbot Rogers, to attend.

The service, which included the hymns "The King of love my Shepherd is" and "Praise, my soul, the King of heaven," was conducted by the vicar, the Rev. W. P. Baddeley, and Dr. Gregg read the lesson from 1 Corinthians, xv.

In a feeling tribute Dr. Dain spoke of a faithful and wise servant. Although Alfred Cox retired from the service of the Association more than 20 years ago he continued his interest in it to the end of his life. He recalled him sitting in the gallery of the Great Hall following the proceedings of a Representative Meeting throughout the day, or writing letters to the *Journal* which showed how up to date even in retirement was his grasp of Association affairs. The speaker mentioned also the struggles of Cox's early life, which, however, never embittered him, his experience as a doctor's dispenser, sleeping under the dispensary counter, the hardships he underwent before he emerged as a medical student, prizewinner in his year. "To-day, with scholarships and other help that a medical student may obtain, such a testing time as Cox underwent is not likely to be repeated, but we may wonder whether the easier way gives better results."

Dr. Dain recalled the remark of Antony, "The evil that men do lives after them; the good is oft interred with their bones." But surely the good had at least an equal chance of survival, and the work of Cox survived in the B.M.A. and in what he had done for his profession. In his early days in his Gateshead practice his energy and drive did much to discover and remedy the weakness of the medical services at that time. He became a councillor in his town and, moreover, a magistrate, not an easy thing for a doctor to become at an early stage in his career. He soon became impressed by the necessity for doctors to get together among themselves, and his career might be said to be a development of the "getting together" idea. It almost seemed as if it was impossible for him to be concerned in any kind of organization without becoming its secretary, and the secretaryships he took on he carried through with the energy and enthusiasm with which afterwards they became so familiar at Headquarters.

The constitution of the British Medical Association as it was fashioned in the early part of this century was to a large extent Cox's work. He rejoiced in its democratic character. If, now, the B.M.A. was looking at its constitution again it was not because of faults in the form in which it was set up then, but because of changes in the conditions of medicine and medical practice. Cox also had had much to do with establishing relationships on a proper footing between the parent Association and its daughter Associations in various parts of the Commonwealth. His visits to Canada and South Africa were of great importance. On both occasions he manifested great qualities of statesmanship, patience, and understanding. It was once said of him that he would have difficulty in getting his own point across because he was so tolerant of the other man's argument, but that was not quite so: he listened to others and then developed his own point of view. In Canada he spent his time in developing friendly associations, and in South Africa he did an even greater work, bringing together men of different outlooks and establishing the solidarity of the profession in a single Association—the Medical Association of South Africa, in affiliation with the B.M.A.

In his later years he endured painful illnesses bravely and cheerfully. To the end he retained his characteristic kindliness and his habit of sending appreciative notes and letters when he felt, as he often did, that appreciation was due. Always they would remember him as a man of complete truth and sincerity and a faithful and wise servant.

C. G. ROBERTS, M.D.

Dr. C. G. Roberts, formerly chief medical officer to the Post Office and deputy Treasury medical adviser, died suddenly in Australia on September 8.

Cecil Gordon Roberts was born on January 2, 1906, and was educated at Uppingham, Emmanuel College, Cambridge, and the Westminster Hospital, where he qualified in 1930. He obtained the Cambridge M.D. in 1939. After holding the appointments of casualty officer and house-physician at the Westminster Hospital, he was resident physician at Ruthin Castle, North Wales, from 1931 to 1935. He then joined the staff of the Post Office as an assistant medical officer, and in 1945 succeeded to the post of chief medical officer and deputy Treasury medical adviser. He relinquished these appointments to go to New South Wales only a short time ago.

H. H. B. writes: Cecil Roberts joined the headquarters medical staff of the Post Office in 1935. Though not addicted, at any rate in later life, to ball games, he was a strongly built man, very fond of walking and climbing, and had once, during a holiday in North Africa, made a sudden divagation into the then not too law-abiding Touareg country and fetched up—to the relief of a harassed consul—at a remote fort of the French Foreign Legion. A man of enthusiasms, Roberts was particularly open to new ideas, and he had a strong interest in the problems of industrial medicine. Owing to the sudden death of Dr. W. Logan Scott he succeeded, relatively early in his Civil Service career, to the post of chief medical officer to the Post Office, and became deputy Treasury medical adviser when the Treasury medical service was established in the last years of the war. He then decided to accept an industrial appointment in New South Wales, a country in whose future he had a great belief, and on the verge of sailing was stricken down with an attack of coronary thrombosis. He accepted this with typical courage and seemed to have made a good recovery. Eventually he arrived in Australia, with a reasonable prospect of many years of able and distinguished service. But, alas, this was not to be. From all who knew him, his widow and two sons will receive the deepest sympathy in their loss.

G. W. WILL, O.B.E., M.B.

H. W. D. writes: The passing of George Will, whose obituary you printed in the *Journal* of September 11 (p. 650), has left a gap in many lives. I remember his kindness and friendliness both at Netley and in Bombay. In the latter place for a time he lived in a bungalow affectionately nicknamed "Pop-gun Cottage" from the fact that it was next door to the G.O.C.'s residence, Gun House. I remember there the delight with which he read *The Specialist* aloud to my wife and me and the glee with which he recalled the fact that in one of his annual confidential reports he had been referred to as "a sane mental specialist." As a personal friend he gave sound advice to junior officers and restored a sense of proportion to those harassed by real or imaginary grievances and climate.

His many friends and patients will have heard with regret of the death of Dr. W. M. O'FARRELL in Guy's Hospital on August 5 at the age of 68. He was a well-known and highly respected general practitioner in Bermondsey, where he had practised for 32 years. William Michael O'Farrell was born in 1886 and was educated at Queen's University, Belfast, where he graduated M.B., B.Ch. in 1913. After graduation he held the appointment of house-surgeon at the Union Infirmary, Belfast, and this was followed by a period in general practice in South Wales. He then held an appointment on the medical staff of Whipps Cross Hospital for four years. In 1922 he took over a practice at Bermondsey and there, by his professional skill, care, and sympathy, won the respect of his patients in a large and growing practice. He had the misfortune, like others of his colleagues in the area, to lose his house in the 1941 air raids, but, transferring to other premises, he carried on under trying conditions through the war years. Although in failing health for the last few years, he continued his professional work until a few weeks before his death. He had a kind personality and never spared himself in the service of his patients. The sympathy of all who knew him will go to his brother and sisters in their loss.—S. B. O'B.

Dr. J. S. MARTIN, who for over 40 years conducted a large industrial practice at Leigh, Lancashire, until he retired 10 years ago, died at Bognor Regis on August 25 at the age of 79. James Sackville Martin was born on November 2, 1874, in a medical atmosphere, his father, who died in 1911, being Dr. John Wise Martin, lecturer in midwifery and diseases of women in the Sheffield School of Medicine, and his grandfather, Mr. James Martin, F.R.C.S.I., being a prominent practitioner in his day in the south of Ireland. His four brothers all entered the medical profession. From Edinburgh University, where J. S. Martin graduated M.B., C.M. in 1895, he went on to St. Thomas's Hospital in 1896 and obtained the London conjoint diploma in the following year. He proceeded to the M.D., with commendation, in 1900, the subject of his thesis being injuries to the cranium and its contents. After graduation he held a number of hospital appointments, including those of clinical clerk to the ophthalmic wards at Edinburgh Royal Infirmary, assistant house-surgeon at Sheffield Royal Infirmary, and house-surgeon at Rotherham Hospital, and for a time he was a ship surgeon. He settled at Leigh at the beginning of the century. During the first world war, in which he served abroad as a captain in the R.A.M.C. in the Mediterranean Command, he married at Valetta, Malta, in 1916, Miss Florence A. Gladstone, whose grandfather was a first cousin of the Rt. Hon. W. E. Gladstone, the great Liberal leader. In addition to the work of his practice Dr. Martin acted for many years as honorary surgeon at Leigh Infirmary and medical officer to the ophthalmic clinic at Leigh. He was chairman of the Leigh Division of the British Medical Association in 1939–40. Outside his professional activities he was a prominent member of the Leigh Literary Society, being vice-president from 1903 to 1905. Several plays which he wrote himself were presented by the dramatic section of the society, and his best-known comedy, *Cupid and Styx*, was produced successfully in Manchester. He was also the author of short stories and poems. He is survived by his widow.—T. G.

We are indebted to Dr. G. H. SHAW for the following appreciation: Friends, and they were very many, will have heard with great regret of the death of Dr. James Sackville Martin. I started in general practice at Leigh in 1904, and since then, until his death, I was privileged to receive his friendship, a very precious thing, continuously for 50 years. His outstanding human quality was his friendliness. This was not a thing to be put on or taken off like a cloak according to circumstances or people, but was given without any qualification, or any idea of self, to all whom he knew: it was the man himself. He understood and sympathized, in an unusual degree for a person not bred in the county, with the qualities of the Lancashire people. We were closely associated during these years; we took over each other's practices at holiday times, and during the first world war we attended each other's patients during our period of service. Increasingly during the years my respect and affection for him grew. His standard of professional conduct was without exception of the very highest, and his advice was sought and valued by all his colleagues and was given without stint. His practice was largely industrial, and he gave scrupulous attention to all his patients, and their interests, joys, and sorrows were his. Apart from his profession, his love was for literature, poetry, and especially drama. His knowledge of these things was very wide. He wrote many short stories for magazines, published several books of verse, and wrote a number of short plays which were produced by the Miss Horniman Repertory Company at the Gaiety Theatre, Manchester. His remarkable memory made it possible for him to quote at length from all these branches of literary art. Dr. Martin's outlook on life was a Shakespearean one. To him all the world was a stage and we the puppets on that stage. The drama of this puppet show, with its infinite variety, engrossed and stimulated him. With his deep knowledge of human strength and frailty, he had charity for all. He leaves behind a very fragrant memory. To his widow, with whom he had a very happy married life, we extend our sincere sympathy.

Dr. R. W. GILMOUR, formerly lecturer in mental diseases at the Middlesex Hospital Medical School and physician in charge of St. Luke's Woodside Hospital, Muswell Hill, died on August 29 at the age of 84. Born in 1870, Richard Withers Gilmour was a student at Durham University before going on to St. Bartholomew's Hospital. He graduated M.B., B.S. in 1895, and very shortly afterwards joined the staff of St. Luke's Hospital for Mental and Nervous Diseases as clinical assistant. He held that position for one year before moving on to gain further experience. In 1901 he returned as assistant medical officer, and remained until 1914, when he resigned in order to take up private practice. But in 1919 he was again appointed to St. Luke's, this time as medical superintendent. For many years Dr. Gilmour had been anxious to establish a psychiatric clinic at a general hospital, and in 1922 he was able, on behalf of the board of governors of St. Luke's Hospital, and through the generous co-operation of the board of governors of the Middlesex Hospital, to establish a small clinic for functional nervous disorders at that hospital. This arrangement was made in close collaboration with, and had the approval of, the Board of Control. He was also at that time the lecturer in mental diseases at the Middlesex Hospital Medical School. Later, in 1930, when the board of governors of St. Luke's opened the new hospital known as Woodside Hospital—which was one of the first to be devoted to the treatment of functional nervous disorders only—he was appointed physician-in-charge, and remained in that position until his retirement in 1935. His total service with St. Luke's and Woodside Hospitals amounted to some 31 years. Two years before his retirement he was elected M.R.C.P. Essentially

a most kindly man, Dr. Gilmour was regarded by his colleagues and patients with sincere affection. His sense of humour was of the kind which helped others, and it remained one of his most attractive qualities during his long and active life.

The sudden death of Dr. MELVIN ROSSIE, of Bathgate, West Lothian, on August 31, has removed from that community one of its best-known and most highly respected citizens. Born in the town on July 5, 1901, William Melvin Brown Rossie received his medical education at Edinburgh, taking the Scottish triple qualification in 1925. He succeeded his father, the late Dr. J. C. Rossie, in the practice on the death of the latter in 1932. In addition to carrying on the practice with great success and acceptance to the patients, he took his full share in civil defence work during the last war and in the work of the local medical and panel committees, besides holding the appointment of deputy medical officer of health of the burgh. He was a man of cheerful and handsome presence with a keen sense of humour and a modesty of nature which endeared him to his patients and to everybody with whom he came in contact.

"His gracious presence upon earth
Was as a fire upon a hearth."

It is indeed a tragedy that such a man should die in his prime and at the height of his career. The deep sympathy of the whole community will go to his widow and family and to his only brother.—H.

The untimely death on September 1 of Dr. MARJORIE BACK has deprived the public health service of one who made a very significant contribution to the preventive medicine of her time, especially in relation to the care of women and children. Marjorie Back was one of a Norfolk family with a strong medical tradition, her father being the late Dr. Herbert Back. Before beginning the study of medicine she entered Newnham College, Cambridge, and read for the natural sciences tripos but did not have the satisfaction of a degree, for at that time the university did not grant degrees to its women students. On coming down from Cambridge, she studied medicine at the London School of Medicine for Women, qualifying M.R.C.S., L.R.C.P. in 1919, and obtaining the London degrees of M.B., B.S. in the following year. Shortly after this she turned her attention to preventive medicine, and passed the Cambridge D.P.H. in 1922. In the same year she proceeded to the London M.D. degree in State Medicine, being awarded the university gold medal. During the next few years Marjorie Back held several public health appointments, notably in Swansea and with the Surrey County Council, and in 1933 she joined the staff of the Middlesex County Council, where as principal assistant medical officer she was destined to spend the remaining years of her working life. She undertook the administration of the maternity and child welfare service and the inspection of midwives, and when war broke out in 1939 she instituted the day nursery service. By her enthusiasm and her hard and devoted work she raised all these services to a very high pitch of efficiency. In 1948 a painful and disabling illness compelled her retirement in the very prime of her life. From then until her death she maintained a lively interest in preventive medicine and especially in the training and work of health visitors, for whom she had a very warm regard. Considerable as were her academic achievements and great the value of her work in Middlesex, it will be for her personal qualities that Marjorie Back will be remembered. She was one of those rare spirits who had the faculty of inspiring genuine affection in those with whom she worked. In particular the midwives and health visitors of Middlesex, whose work on occasion she had to criticize, simply loved her. A woman of the highest principles from which nothing could deflect her, she gained her objectives by her kindness, gentleness, and sweetness of disposition. High among her qualities was courage, as shown by her gentle humour and philosophical attitude during the last six years to the long and painful illness that ultimately ended her life. It is some satisfaction to know that the Middlesex County Council intend to keep green her memory by naming the Bedfont Health Centre, shortly to be erected, the "Marjorie Back Clinic."—H. M. C. M.

The death of Dr. A. WALLACE JOHNS on September 6 has left a gap which will be felt for a long time to come in the life of Merton and Morden, where he was medical officer of health, and indeed in local government circles in north-east Surrey generally. Born on October 1, 1903, the younger son of the late Alderman W. J. Johns, several times mayor of Helston, Cornwall, Arthur Wallace Johns studied medicine at the London Hospital, qualifying in 1928. Five years later he took the D.P.H. of the English Royal Colleges. After holding the appointments of receiving-room medical officer at the London Hospital and house-physician at the Seamen's Hospital, Greenwich, he then became, first, assistant resident medical officer and later resident medical officer at the City of London Maternity Hospital. He obtained his first post as medical officer of health, to the Erith Urban District Council, in 1934, leaving there to become medical officer of health for the Merton and Morden Urban District in 1940. Since 1949 he had held the additional appointment of divisional medical officer under the Surrey County Council. In Merton and Morden he soon endeared himself to an ever-widening circle, official and social. His friendliness and kindliness were notable in every sphere of his many activities, and this was borne out by the great popularity he enjoyed with his staff and among the masters, mistresses, and scholars of the local schools. He was also a very courageous man, as was shown not only during his recent illness but also by the prominent part he took in civil defence during the last war. He was one of the first medical officers of health to be called into action in this country to deal with air raid casualties, at an incident which occurred on August 16, 1940, only four months after he had been appointed to Merton and Morden. Casualties were spread over a distance of two miles, and as officer-in-charge of first-aid parties and civil defence ambulances Dr. Johns was unsparing in the work of helping the injured. During the long succession of air attacks which Merton and Morden suffered he was out nightly at the scene of many incidents. One of the most memorable of these was in February, 1944, when the maternity wing of Nelson Hospital had to be evacuated after an attack in which incendiary bombs were used. For relaxation he turned to golf, and made many friends among the members of the golf clubs in north-east Surrey. All who knew him mourn his passing at such an early age and extend their sympathy to his widow.—H. M.

Dr. R. W. ANNISON, a well-known North London general practitioner, died suddenly on September 9 at the age of 68. Richard William Annison was born on April 1, 1886, and, after qualifying M.R.C.S., L.R.C.P. in 1910, held the appointments of house-physician and house-surgeon at the Middlesex Hospital, where he received his medical education. He then settled in practice in North London, first at Holloway and then, a few years later, at New Southgate, where he remained for the rest of his life, except for his period of service in the R.A.M.C. in the first world war. For many years he was a medical officer to the Passmore Edwards Hospital at Wood Green.

We are indebted to Mr. T. TWISTINGTON HIGGINS for the following appreciation: As one who was closely associated with R. W. Annison for many years, I would like to pay a brief tribute to his memory. Annison was an outstanding doctor, inspiring complete confidence in patients by his skill and constancy, and enduring respect and friendship in colleagues by his integrity and lovable personality. One always felt better for meeting this wise and gentle man with his imperturbable demeanour and quiet humour, his unfailing loyalty and considerate understanding. He will be sadly missed by many, and especially by those of us who had good cause to know his sterling qualities and who were his privileged comrades for so many years.

Medico-Legal

FINED £100 FOR DRUGS OFFENCES

Dr. James McKenzie, of Rochdale Road, Middleton, Lancs, was fined a total of £100 and ordered to pay 15 guineas costs when he pleaded guilty at Middleton Magistrates' Court on September 13 to summonses, respecting five patients, for contravening Section 8 of the Dangerous Drugs Regulations, 1953, by obtaining a "float" of "physeptone" (amidone).

Instead of handing the prescription to the patient and allowing him to collect it from a chemist, the defendant, according to the prosecution, had himself taken the prescription to the chemist, collected the drugs, and then misapplied them. In some cases the patient in whose name the drugs were prescribed was not in need of these tablets, and in other cases only a portion of the prescription was supplied to a particular patient and the residue was supplied to other patients. If the doctor wanted a "float" of this particular drug he could have obtained it on a prescription issued in his own name. He would then have had to enter it in his own dangerous-drugs register. There was no suggestion that the drugs were used for addiction purposes.

Two police inspectors found that in the period December 15, 1953, to March 31, 1954, chemists in Middleton had dispensed amidone in respect of 253 prescriptions, and 96 of these had been prescribed by this doctor. In a statement to the inspectors, Dr. McKenzie said he was genuinely unaware of the fact that these tablets were subject to the exigencies of the Dangerous Drugs Act. "I knew that the injection of physeptone, supplied in ampoules, was on the list of dangerous drugs, and that strict measures had had to be introduced in relation to linctus physeptone in view of the potential danger which it had been found to hold for children. Why I should have held the tablets to be otherwise is difficult to explain, but I got into the habit of prescribing them with increasing frequency from about September, 1953; it was a drug which I had never used previously.

"I cannot recall having used these tablets for treatment—other than in a few isolated cases where another doctor initiated the treatment—until September last, and I have since then drifted into using them in large quantities spurred on by their dramatic effect.

"Advertisement material from the manufacturers listed the advantages of physeptone and 'dromoran' (methorphinan) in their various forms, but none of the documents gave the slightest indication that these drugs were scheduled under the Dangerous Drugs Act. I think this is most unfair to doctors, who are confronted with an ever-increasing range of new drugs, and under such circumstances omissions of this kind are definitely misleading. I got a comprehensive list of the actual persons who were involved in the investigation. I became genuinely attached to the people who for different reasons were not able to procure the medicine and drugs which I had occasion to prescribe for them. I became interested in their health, and it frequently made me very depressed to enter the home of one of these and find that my prescription, issued a week earlier, still lay where I had left it. The reason for it was that these poor people had nobody sufficiently interested to fetch their medicine. I began to hand in their prescriptions for them. This led to my collecting them and finally giving the chemist the prescription and taking the drugs with me."

For the defence it was emphasized that the whole trouble arose out of the doctor's desire to assist elderly patients who were incapable of helping themselves. He found that, having prescribed in advance, the medicine was not required or the quantity was not required, which left him with some of it on his hands. He used this in a perfectly proper way by supplying it to other patients who required it. The drugs were for use in his practice and not for any illegitimate or illicit purpose.

The magistrates imposed fines of £20 in respect of each of the five cases, and granted the doctor three months in which to pay.

DEATH FOLLOWS SUCKER FAILURE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

At 11.30 p.m. on August 30, 1954, Douglas Paul Franks, a healthy little boy aged 7, was admitted to Wordsley hospital with a diagnosis of acute appendicitis. The diagnosis was confirmed by Dr. C. G. Shaw, who began the operation of appendicectomy about one and a quarter hours later. The anaesthetic was uneventful throughout the operation, which lasted about one hour and, in spite of difficulty in closing the peritoneum owing to distension, was wholly successful.

At the completion of the operation and after the anaesthetic stopped, the patient vomited. Dr. Shaw had him put into a steep Trendelenburg position and tried to suck out the pharynx by means of a sucker which had been tested before the operation and had been found satisfactory during the operation. The sucker failed and could not be restarted. A second sucker was fetched from another theatre, but the electrical connexions would not fit. At this stage the patient stopped breathing, and a third sucker, from the anaesthetic room, was too weak to have any effect. Finally, the pharynx was cleaned as well as possible by swab, the trachea was intubated, and the vomitus sucked out by mouth, but in spite of intracardiac nikethamide, artificial respiration, cardiac massage, and adrenaline and procaine injected into the heart the boy did not revive.

At the inquest before the deputy coroner for south-west Staffordshire the jury added to their verdict of death by misadventure a rider that all theatre pumps and sockets should be standardized and stricter supervision exercised in the maintenance of all equipment. That they did so is not surprising in face of such a tragic example of the result of such vitally important apparatus failing.

Vital Statistics

HARWELL WASTE IN FOREST OF DEAN

[FROM A SPECIAL CORRESPONDENT]

Authorization has been given by the Minister of Housing and Local Government under the Atomic Energy Authority Act, 1954, for the disposal of solid wastes from Harwell into four disused mines in the Forest of Dean. The waste is to consist only of apparatus, fittings, and containers having a level of activity comparable with that normally dealt with in low-level laboratories. The authorization requires that the authority should monitor streams and other sources of water in the neighbourhood. As miners are working seams of coal under the bottom of these mines, and as the three local authorities of the area obtain their drinking water from springs and wells around the coal basin, it is not surprising that considerable local concern should be expressed both for the safety of the miners and the water supplies of the area. A conference of local authorities and other bodies was held and a request made that high-ranking officials of the Ministry and representatives from Harwell should meet a deputation before any depositing takes place.

Sir John Cockcroft and other research workers from Harwell, together with Dr. T. Robertson of the Geological Survey, addressed a meeting of local representatives at Coleford on September 14. Sir John said that the radioactive effluent from Harwell was discharged with complete safety into the River Thames, and radioactive gases were discharged into the atmosphere from chimney-stacks. Some wastes were stored indefinitely in safe containers at Harwell and others dealt with by sea disposal, the most highly active being submerged over the Atlantic shelf. Sir John emphasized that the waste comprised only apparatus, fittings, and containers having a level of activity comparable with that dealt with in low-level laboratories and contained no highly

active material. He said that about 60 lorry loads had accumulated, and this would be followed by one or two lorry loads per week. The total activity of the waste was small and a hundred times less than that already present naturally in the top 50 yards (46 m.) of soil in the central basin of the coalfield. Operations would be controlled by monitoring, so that the activity in the water in the basin would not be raised above the internationally accepted drinking-water tolerance. This tolerance is based on the assumption that 4 pints (2.3 l.) of this water are drunk every day for 70 years. Even if the water percolates to the working pits or to the lower series from which drinking water is drawn, both of which are most unlikely, according to the Geological Survey, no harm would result. In reply to a question, Dr. Marley, one of Sir John's team, said that the level of concentration that would be safe for miners to come in contact with would be 1,000 times higher than what is safe for drinking.

Dr. T. Robertson, the geologist, explained that the pits in question were in the central basin of the coalfield, and this contained a large quantity of static water which did not leak into the lower and outer part of the basin because there was a thick layer of impervious Pennant sandstone between the two.

The public health aspects of this dumping appear to be covered. The radioactivity of the waste has to be seen in perspective against the ever-present natural radioactivity, yet there are bound to be misgivings lest an error be made and material of higher activity finds its way into the dump, especially in view of the extreme persistence of this type of pollution.

The Forest of Dean is a geographical entity and renowned for its scenic beauty. It was a depressed area in the 'thirties, and a very active development association has coaxed industry into it to compensate for the gradual dwindling of the labour employed in the mines. It is not surprising, therefore, that there should be a strong local objection to allowing the area to become known as a national dump for material which is popularly regarded as so sinister, however small the real hazard.

Week Ending September 11

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 313, whooping-cough 2,014, diphtheria 12, measles 1,083, acute pneumonia 262, acute poliomyelitis 78, dysentery 219, paratyphoid fever 21, typhoid fever 4.

Infectious Diseases

Only small fluctuations were recorded in the trends of infectious diseases in England and Wales during the week ending September 4. The largest were declines of 124 for measles, from 1,699 to 1,575, and 50 for whooping-cough, from 2,038 to 1,988.

The largest decrease in the number of notifications of measles was 73 in Lancashire, from 485 to 412, and the largest increase was 36 in Durham, from 203 to 239. 360 cases of scarlet fever, 11 more than in the preceding week, were notified, and no large variations were recorded in the local trends. The largest fall in the incidence of whooping-cough was 23 in Northumberland, from 67 to 44. 11 cases of diphtheria were notified, and these were 7 more than in the previous week. 3 cases were notified in Liverpool C.B. and the remainder were spread over 8 counties.

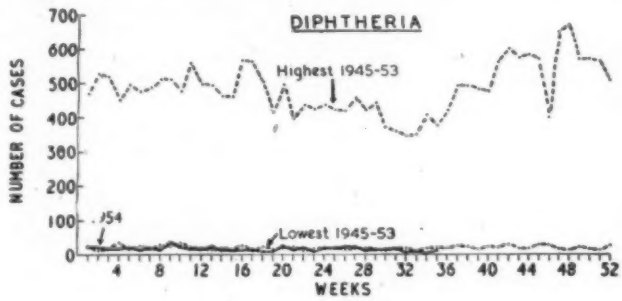
The largest outbreak of paratyphoid fever was 6 cases in Yorkshire West Riding (Queensbury and Shelf U.D. 6). 6 cases were also notified in Lancashire, and five counties contributed the other 6 notifications.

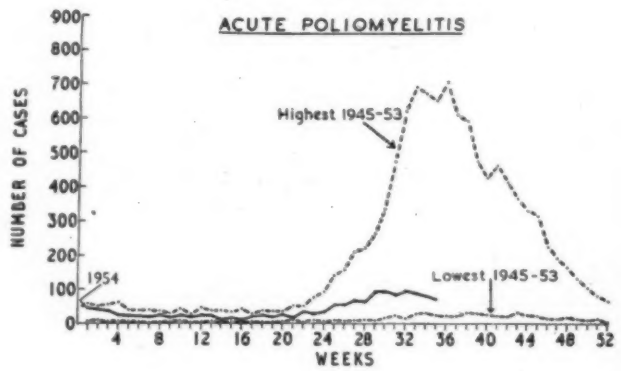
71 cases of acute poliomyelitis were notified. These were 10 fewer for paralytic and 2 more for non-paralytic cases than in the preceding week. The largest returns were Durham 8 (Sunderland C.B. 4), London 6 (Woolwich 2), Kent 5 (East Ashford R.D. 2), Essex 5, and Lancashire 4.

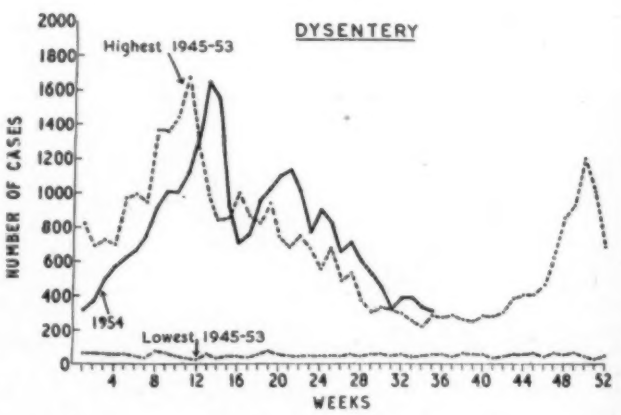
317 cases of dysentery, 24 fewer than in the preceding week, were notified. The largest centres of infection were London 51 (Islington 12, Finsbury 11), Lancashire 47 (Liverpool C.B. 14, Swinton and Pendlebury M.B. 12), Staffordshire 44 (Stone R.D. 31), Yorkshire West Riding 29, and Dorset 20 (Dorchester R.D. 19).

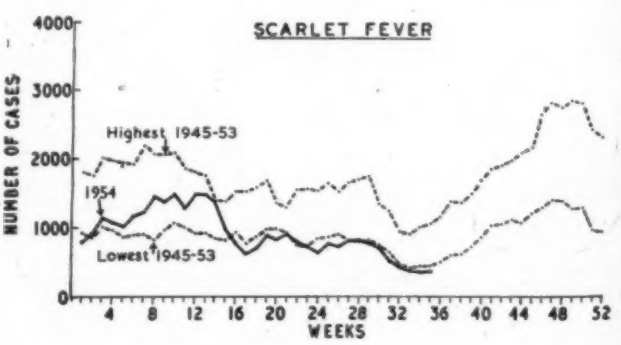
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - - -, the figures for 1954 thus ———. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **September 4** (No. 35) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	11	1	3	0		20	3	6	0	
Dysentery	317	51	191	3	2	205	43	94	8	10
Encephalitis, acute	3	0	1	0		5	1	1	0	
Enteric fever										
Typhoid	6	1	0	0	0	9	0	1	2	0
Paratyphoid	18	2	4	0	23	11	1	3	1	1
Food-poisoning	248	14		5		256	24		1	
Infective enteritis or diarrhoea under 2 years				13	17				19	59
Measles*	1,575	63	142	26	40	802	27	30	21	30
Meningococcal infection	26	1	16	0	1	26	2	6	0	3
Ophthalmia neonatorum	34	0	6	1		27	1	4	0	
Pneumonia†	229	16	95	4		183	12	119	6	1
Poliomyelitis, acute:										
Paralytic	44	2	9	0	3	123	9	26	10	16
Non-paralytic	27	4				101	7			
Puerperal fever§	262	41	16	1		246	38	11	0	
Scarlet fever	360	23	83	17	16	483	26	123	13	26
Tuberculosis:										
Respiratory	621	60	116	34				131	22	
Non-respiratory	80	6	20	13				19	6	
Whooping-cough	1,988	109	125	14	10	4,058	354	516	28	65

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	1		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	1	0	2	6	2	0	0	0
Influenza	2	0	1		0	0	0	0	0	1
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	132	14	18	6	4	115	14	17	10	3
Poliomyelitis, acute	3	1		1	0	8	0	1		0
Scarlet fever		0	0	0	0		0	1	0	0
Tuberculosis:										
Respiratory	81	8	10	1	5	84	14	8	1	3
Non-respiratory		1	1	1	0		1	1	0	1
Whooping-cough	0	0	0	0	1	2	0	0	0	0
Deaths 0–1 year	191	21	18	3	10	162	31	22	4	9
Deaths (excluding stillbirths)	4,498	627	499	88	149	4,146	595	490	99	107
LIVE BIRTHS	7,081	1105	914	210	372	7,289	1081	786	200	385
STILLBIRTHS	196	22	16			185	25	30		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Mental Patients.—The Board of Control's annual *Report to the Lord Chancellor* (H.M.S.O., price 6d. net) discusses the question of the elderly mental patient. At the end of last year almost 29% of the 150,000 patients in mental hospitals in England and Wales were 65 years of age and over. About two-thirds of them were women. Fifteen years ago the percentage was 17.5. This increase, says the report, is only in part due to the ageing of the population; other important reasons are loss of beds in former public assistance institutions and social factors such as the increased employment of women and housing shortages. According to standards of space prescribed by the Ministry of Health, the mental hospitals are still badly overcrowded, to the tune of nearly 19,000 patients. This unsatisfactory situation, particularly so far as elderly patients are concerned, would be eased, it is suggested, by the provision of more domiciliary services, day hospitals, social clubs, and beds both in the hospital service and outside it. Commenting on the widespread feeling that certification and admission to mental hospitals could be avoided in many instances if suitable accommodation for old people were available elsewhere, the report suggests that some of these patients might be given short-term treatment in special geriatric centres and then be returned home, while others might go to chronic sick wards or long-stay annexes. One favourable factor is that the outlook for old people with mental symptoms is much brighter than formerly: in many cases active treatment can lead to rapid recovery. A survey of aged persons admitted to six mental hospitals showed that 38% were discharged within a year. The nursing situation in mental hospitals is still serious. At the end of 1953 there were 7,712 male and 4,610 female trained nurses, a slight rise on the previous year; but over 1,000 mental hospital beds could not be used during the year because of the shortage of nurses, and there is now a decline in the number of student nurses of both sexes taking up mental nursing. Because of the advanced age of the mental hospital population the death rate is high: in 1953 it was 7.9%. Tuberculosis at 5.5 per thousand was the lowest figure so far. There were 22 cases of the typhoid fevers, 731 of dysentery (mostly mild), and 4 of pellagra.

The Best Use of M.M.R.—In a Medical Research Council report, commended to hospital boards by the Ministry of Health, the best uses of mass miniature radiography are now defined as the examination of symptomatic cases referred by doctors and the comprehensive surveying of "black spots." M.M.R. units should confine themselves to spotting the abnormal case and not attempt to provide full diagnostic facilities. Except in special circumstances, the re-examination of the same population at intervals of less than three years simply to detect new cases of pulmonary tuberculosis is condemned as unjustifiable on both medical and economic grounds. Surveys show that in static populations, if active cases are isolated on discovery, the yield of new cases falls sharply on re-examination. The regular examination of teachers, medical students, nurses, and food-handlers is advised. The report is the work of a subcommittee of the Medical Research Council's committee for research on social and environmental health. Other recommendations are concerned with technical matters such as methods of recording statistical data and the standardization of terminology. In 1953 there were 70 M.M.R. units in England and Wales (62 mobile and 8 static) which screen between them about three million people each year.

Medical Research in Ireland.—Once again the Medical Research Council of Ireland has had to complain about the uncertainty of its financial provision. It depends almost entirely on grants from the Minister for Health which are guaranteed for only short periods. Last year £21,000 was provided for general research and £3,500 in connexion with the National Tuberculosis Survey. In its current annual

report the Council points out how difficult it is to plan long-term research on this basis, and asks if its record over the last 17 years does not justify some more permanent arrangement. During 1953 a trial of isoniazid sponsored by the Chemotherapy Research Unit and the work of the National Tuberculosis Survey were completed; a field survey of children's dietary habits in relation to dental caries was finished, and the results are being analysed; the high incidence of goitre in South Tipperary was established as being due to iodine deficiency, and iodized salt recommended—a policy which is "apparently being gradually adopted." Other work has been concerned with the safe disposal of radioactive isotopes, cortisone, various scientific investigations, and the improvement of the status of laboratory technicians. The Council is proposing to review the basis of training and other grants, as applications from younger workers are falling off.

Collegium Internationale Allergologicum.—The Collegium, a newly founded international association for those engaged in research on the clinical and scientific problems of allergy, has as its principal object the promotion of friendly scientific co-operation among its members. The College will organize informal symposia and meetings for a limited number of participants, at which it is hoped that trends of future research will be discussed as well as the results of the latest work. The first symposium is being held in London next month (October 12–16) at the Ciba Foundation. The president of the College is Dr. D. HARLEY, and the British founder members are Dr. C. J. C. BRITTON, Dr. R. R. A. COOMBS, Sir HENRY DALE, Dr. J. FREEMAN, Dr. C. P. GILES, Professor J. R. MARRACK, Dr. W. PAGEL, and Professor C. RIMINGTON. The secretary is Dr. P. KALLÓS, Sundstorget 3, Helsingborg, Sweden.

Wright–Fleming Institute.—Sir ALEXANDER FLEMING, F.R.S., who is 73, is due to retire at the end of this year from his post as the head of the Wright–Fleming Institute of Microbiology at St. Mary's Hospital Medical School, London. An advertisement for a successor, at a salary of £3,000, appeared in our advertisement columns (page 40) last week.

Sir Stewart Duke-Elder, director of research at the Institute of Ophthalmology, London, was awarded the Gonin Medal for outstanding work on eye diseases at the 17th International Congress of Ophthalmology held recently in Montreal and New York.

COMING EVENTS

Radio and Television.—There will be two short television programmes next week in connexion with the centenary of St. Mary's Hospital Medical School: on Thursday, September 30, at 8.35 p.m. a 10-minute talk by a member of the hospital staff, "Better No Medicine . . ."; on Friday, October 1, at 10 p.m. a 30-minute camera report on a house-surgeon at work. On the Home Service at 8.15 p.m. on Friday, October 1, there will be a 45-minute broadcast on "The Skin." It deals with such questions as hormone and vitamin creams, baldness, and the relationship of mental factors to skin disease. The programme is produced by NESTA PAIN, with advice from Professor J. R. SQUIRE and Dr. D. STAFFORD-CLARK.

Sheffield Medical School.—The opening sessional address of the Faculty of Medicine, Sheffield University, will be given by Sir LIONEL WHITBY at 5 p.m. in the Firth Hall on October 12. His subject will be "A Doctor Looks Back."

Study Circle on Medical Statistics.—First monthly meeting of 1954–5 session, at Westminster Medical School, September 28, at 6.45 p.m. Dr. W. P. D. LOGAN will read a paper on "Some Developments in National Vital Statistics." Visitors welcome. Information from Mr. M. P. CURWEN, St. Bartholomew's Hospital, London, E.C.1.

Institute of Dermatology.—Exhibition on animal ringworm infection, October 1 to 25, at St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London, W.C.2.

Moynihan Lecture.—Dr. OSWALDO P. CAMPOS (president of the joint meeting of Brazilian and Latin American Orthopaedic Associations, 1954) will lecture at the Royal College of Surgeons, Lincoln's Inn Fields, on "One Thousand Cases of Bone and Joint Tuberculosis," at 5 p.m. on October 14.

Bengué Memorial Lecture.—Dr. FRANKIS T. EVANS will lecture on "The Veins and the Anaesthetist" on October 21 at 5 p.m. at the Royal Institute of Public Health and Hygiene, 28, Portland Place, London, W.1. Admission free.

Thomas Vicary Lecture.—Sir GORDON GORDON-TAYLOR will lecture at the Royal College of Surgeons, Lincoln's Inn Fields, on "The Life and Times of Sir Charles Bell," at 5 p.m. on October 28.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, September 27

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. J. G. Bonnin: Fractures of the Ankle Joint; 6.30 p.m., Mr. J. E. A. O'Connell: Intervertebral Disk Protrusion with Involvement of the Spinal Cord.

Tuesday, September 28

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 9 p.m., Dr. Michael P. Ward: Ascent of Everest.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. L. P. Le Quesne: Paralytic Ileus; 6.30 p.m., Mr. A. J. Gardham: Carcinoma of the Tongue and Mouth.

Wednesday, September 29

ABORTION LAW REFORM ASSOCIATION.—At Conway Hall, Red Lion Square, London, W.C., 6 p.m., annual general meeting. 7.30 p.m., public meeting. Dr. Dorothea M. Kerslake: Is Reform Needed? A discussion will follow.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. F. C. W. Capps: Tumours of the Nasopharynx, their Classification, Diagnosis, and Treatment; 6.30 p.m., Mr. H. J. Seddon: Peripheral Nerve Injuries.

Thursday, September 30

●HUNTERIAN SOCIETY.—At 41, Portland Place, London, W., 6 to 8 p.m., annual party.

MEDICAL SOCIETY OF LONDON.—5 p.m., Lloyd Roberts Lecture by Dr. Charles Singer: How Medicine Became Anatomical.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. Dillwyn M. E. Thomas: The Surgery of Pulmonary Tuberculosis; 6.30 p.m., Dr. Walter M. Levitt: The Basic Principles of Radiotherapy.

Friday, October 1

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Dowling.

INSTITUTE OF DISEASES OF THE CHEST, Brompton Hospital.—5 p.m., Dr. N. C. Oswald. Clinical demonstration.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m. Mr. Philip H. Newman: Recurrent Dislocations of Joints; 6.30 p.m., Professor A. G. R. Lowdon: Surgery of the Spleen.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., Dr. R. Forbes: Recent Developments in Medical Litigation.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Herriott.—On September 12, 1954, to Mary (formerly Gunning), M.B., B.Ch., wife of S. Dunn Herriott, M.B., B.Ch., of 2, Maidstone Road, London, N., a son—Peter Francis.

Stewart.—On September 10, 1954, to Mary (formerly Reynolds), wife of J. Stewart, M.B., Ch.B., of 6, Bourne Vale, Hayes, Bromley, Kent, a daughter.

MARRIAGES

McCarthy—Moore.—On September 8, 1954, at The Lady Chapel, University Church, Dublin, Dr. Derry McCarthy, of Midleton, Co. Cork, to Dr. Eva Moore, of Freshford, Co. Kilkenny.

Mills—Evans.—On July 30, 1954, at Llandaff Cathedral, David John Mills, M.A., of Clevedon, Somerset, to Mary Evans (formerly Kane), M.D., of Nottage, Glamorgan.

DEATHS

Batteson.—On September 14, 1954, at his home, 1, Devereux Drive, Watford, Herts, Carol Luther Batteson, M.R.C.S., L.R.C.P., aged 82.

Churchill.—On September 16, 1954, at Mentone, France, Stella Churchill (formerly Myers), M.R.C.S., L.R.C.P., D.P.H., of 14, Park Village East, London, N.W., aged 71.

O'Brien.—On August 29, 1954, at Bensham General Hospital, Gateshead, Co. Durham, Donal Hugh O'Brien, M.B., B.Ch.

Vakil.—On September 4, 1954, Pestonji Rustomji Vakil, M.B., B.S., Lieutenant-Colonel, I.M.S., retired, of 2, Eversley Park Road, London, N.21.

Wallace.—On September 9, 1954, at Cardiff Royal Infirmary, Thomas Wallace, M.B., B.Ch., of 69, Newport Road, Cardiff.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Oestrogens and the Bust

Q.—*Is ethinyloestradiol used locally or systemically of any value for flat-chestedness in women due to the failure of normal development of the breasts in adolescence? Is there any danger of malignant changes in the breast as a result of the continued use of stilboestrol creams advertised to the public?*

A.—In general, it can be said that ethinyloestradiol used either locally or systemically is of little or no value for flat-chestedness due to failure of breast development in adolescence. Usually such hypomastia, unaccompanied by other evidence of hypogonadism, is due to target-organ failure—that is, to absence of responsive mammary tissue or to an inadequate response of such tissue. In addition, insufficiency of adipose tissue in the breast is commonly found in these cases. Only when there is evidence of oestrogen deficiency is it likely that oestrogen treatment will have much effect.

There is no direct evidence that the continuous application of stilboestrol creams leads to malignant changes in the breasts, but the results of animal experiments leave no doubt that such changes are a possibility. Consequently the continued use of these creams is, to say the least, highly imprudent, as well as unlikely to achieve any useful results.

Cold and Surgical Shock

Q.—*We used to be taught that cold was one of several factors in the production of surgical shock, and that warmth was an important part of its treatment. What is the generally accepted teaching on this subject now? When major surgery is done under conventional anaesthesia, is the temperature of the theatre and patient still considered of importance? In particular, is the cooling of abdominal viscera not now considered of any consequence?*

A.—It is true that there has been some change of viewpoint regarding the relationship of cold and shock; the older idea that warmth was an important part of the treatment of shock has been much criticized. Put very briefly, and therefore inadequately, cold is now regarded as being produced by shock whereas formerly it was believed that shock was produced by cold. It is, of course, necessary to draw a distinction between surface temperature, which is so obvious to the observer, and the inner temperature of the body. In this way the surface cooling, brought about by contraction of the peripheral vessels, may be regarded as an indication that a protective mechanism is at work tending to counteract the fall of blood pressure and to prevent wasteful use of oxygen. To interfere with such a natural means of protection by artificially warming the surface would thus appear to be actually harmful, for more blood will then be diverted to the surface vessels with further lowering of the general blood pressure. Some years ago Blalock and Mason showed that the survival time of dogs subjected to standard degrees of shock was considerably prolonged by cooling and shortened by overheating, but long before this it had been suggested by Lake that a shocked patient would be better artificially cooled than warmed.

Excessively hot operating theatres, with specially heated operating tables, are no longer seen, but patients do not suffer from surgical shock in consequence. The viscera themselves present a somewhat different problem, since they are internal structures whose vessels do not respond to cold in quite the same way as the skin; nevertheless, in dealing, say, with intestine exposed for a considerable time it is much more important to prevent drying of the surface (perhaps by wrapping the bowel in an impervious membrane) than it is to prevent cooling, although the latter effect will of necessity be associated.

There are, of course, many instances of the deliberate use of cold in treatment, usually locally, but these fall outside the scope of this question.

Cigarettes and Cancer

Q.—*Is there any information on the nicotine content and carcinogenic properties of different brands of cigarettes? Do filter tips prevent nicotine and carcinogens from being absorbed?*

A.—There is an immense and very scattered literature on the composition of tobacco in its various forms, but I do not know of any summary of the data on the nicotine content of different brands of cigarettes. We have no data as to the comparative carcinogenic power of different brands of cigarettes.

All filters, including the stump of the cigarette, will stop a certain amount of nicotine. Experiments on the power of various filters to arrest carcinogenic factors are in progress in various laboratories.

Thiacetazone in Tuberculosis

Q.—*Thiacetazone has been reported to have a very definite beneficial effect in African pulmonary tuberculosis.[1] Can you tell me if thiacetazone gives rise to resistant tubercle bacilli, and, if so, how rapidly and to what extent? Does thiacetazone prevent or delay resistance to streptomycin, P.A.S., or isoniazid?*

A.—Thiacetazone does give rise to resistant tubercle bacilli, but how often I do not know.

Professor K. A. Jensen, of Copenhagen, has reported[2] that the combination of streptomycin plus thiacetazone (TB 1), in a series of cases of pulmonary tuberculosis, delayed streptomycin resistance but did not by far come up to the high standard of efficiency of streptomycin plus P.A.S. I have no information about the prevention of isoniazid resistance, though from the above report thiacetazone would be expected to be less efficient than either streptomycin or P.A.S. for this purpose.

It seems most inadvisable to use thiacetazone alone in pulmonary tuberculosis; indeed, it is doubtful whether this drug is worthy of use at all, even in combination. If it is desired to use only oral therapy, then isoniazid plus sodium P.A.S. could be given. The preliminary results in the Medical Research Council's trial[3] suggest that it may be possible to reduce the daily dose of sodium P.A.S. to 10 g.

REFERENCES
1 *E. Afr. med. J.*, 1952, **29**, 339.
2 *Bull. Un. int. Tuberc.*, 1952, **22**, 16.
3 *British Medical Journal*, 1953, **2**, 1005.

Lesions of the Conus Medullaris

Q.—*Is it possible to distinguish clinically between lesions of the conus medullaris and the cauda equina? What spinal segments are contained within the conus? From what source is the blood supply of the conus derived?*

A.—Although the clinical differentiation of lesions of the cauda equina and conus medullaris is sometimes difficult, it is often possible. In lesions of the cauda equina root pains are frequent and severe and involve the distribution of the lower lumbar and sacral roots—unilateral or bilateral—sciatic pain being particularly common. Such pain is infrequent in lesions of the conus. Muscle atrophy, loss of power, anaesthesia, and reduction of tendon reflexes in the lower limbs are more marked and develop earlier in lesions of the conus than in those of the cauda equina. Likewise disturbance of vesical and rectal control occur earlier and are more severe in conus lesions. The conus medullaris is the inferior extremity of the spinal medulla and contains the last three sacral and the coccygeal segments. Its blood supply, like that of other segments, is provided by the single longitudinally disposed median anterior spinal

artery and the paired posterior spinal arteries each in two branches, one anterior and one posterior to the line of attachment of the posterior nerve roots to the spinal medulla. At each segmental level these descending branches of the vertebral artery are reinforced by lateral spinal arteries, branches of the appropriate segmental vessel, which enter the spinal canal through each intervertebral foramen and send branches to the spinal medulla along the anterior and posterior nerve roots.

Antibiotics in Whooping-cough

Q.—*What is the best antibiotic to use in whooping-cough? What dosage should be employed, and how effective is such treatment? How great are the risks of serious complications of treatment such as agranulocytosis?*

A.—Most observers agree that chloramphenicol, aureomycin, and terramycin appear about equally effective in the treatment of whooping-cough if given in the initial stage, and also in the paroxysmal stage provided treatment is begun before the end of the second week of the disease. Success is shown by a reduction in the number and severity of paroxysms. Failures, however, are only too common, particularly if cases are not treated early.

The usual dosage is based on weight, and the optimum total is generally accepted to be for chloramphenicol 50–100 mg., for terramycin 20 mg., and for aureomycin 25 mg. per kilo per day. The course of treatment should last for eight to ten days. In view of accumulating evidence of the danger of chloramphenicol, especially if given in prolonged or repeated courses, it would appear best to restrict its use to infants and to young children with severe attacks.

As the synthesis of vitamin B in the gut may be interfered with by antibiotics it is usual to prescribe preparations containing the major factors of the vitamin-B complex. From one to three tablets daily of a preparation containing aneurine hydrochloride 1 mg., riboflavin 1 mg., and nicotinamide 15 mg. should suffice. The tablets should be crushed for infants.

Ion Exchange Resins in Cardiac Oedema

Q.—*What place have cation exchange resins in the treatment of cardiac oedema? I have a patient who is not responding well to mercurial diuretics, a low sodium diet, and aminophylline. If resins should be used, please give details of their administration.*

A.—A low sodium intake is of value in the treatment of cardiac oedema, but the necessary reduction of its salt content often makes the diet unpalatable. Cation exchange resins may be used to reduce the available sodium in an otherwise normal diet. Resins do not abstract sodium from body fluids. The amount of sodium absorbed on the resin is proportional to the sodium content of the diet. "Katonium" and "resodex" are two resins which can act in this manner: 15 g. thrice daily may be mixed with food or given in a draught at the time of a meal. Unfortunately, these substances are only of temporary value and are not recommended for long-term administration, as low sodium states may result, manifested by rising blood urea and circulatory depression. Potassium deprivation is largely avoided by a 25% potassium charge on the resin, but serum potassium should be checked during treatment. If treatment is long continued calcium deprivation (osteoporosis) is a risk. Administration of excess calcium orally may correct this effect, but in so doing it diminishes the sodium-absorbing power of the resin, thus reducing its therapeutic value.

NOTES AND COMMENTS

Intravenous Therapy in Infants.—Dr. MORRIS WITKIN (Johannesburg) writes: With regard to the best route for giving saline infusions to infants ("Any Questions?" May 15, p. 1166), I join hands with Dr. Lorna G. Macdougall (*Journal*, July 31, p. 314) in sponsoring the intraperitoneal route. In the athreptic infant, where life is at a low ebb, the intraperitoneal route is the procedure of choice. I have employed this method in over 100 such cases in the infant wards of Germiston Hospital, Johannesburg, with gratifying results. Depending on the infant's weight, 500 ml. or more of half-strength normal saline, Ringer's, or Hartmann's solution are run into the peritoneal cavity at blood heat. This is done by immersing the lower loop of tubing in a basin of hot water. With the bladder empty, bowels undistended, and strict asepsis, a 16 gauge 2-in. (5-cm.) needle with short bevel is smartly pierced into the peritoneal space in the median line, ¾ in. (2 cm.) below the umbilicus. The fluid is run in until the abdominal contour changes from hollow to flat. This takes 15 minutes. The "repair" fluid is rapidly absorbed into the blood stream, half in the first hour and the rest within a day. To the uninitiated it is indeed a revelation to see a moribund, depleted infant soon transformed into an alert child following this technique. The intraperitoneal route was much in vogue when I was a houseman, some 32 years back. It has lost popularity because it is erroneously believed that it could puncture bowel, cause shock or peritonitis, or inflame abdominal organs. With proper care this never occurs. As a rapid means of restoring fluid and electrolyte balance the intraperitoneal route is often a life-saver. It is safe, quick, effective, painless, and without shock. In the marasmic and moribund infant this route is preferable to venoclysis, with its time-consuming cut-downs which often fail to negotiate the threadlike veins or stay in them. The intraperitoneal route is the forgotten ally of parenteral therapy. It claims rightful recognition in our armamentarium.

Local Analgesics for Scalds.—Dr. W. C. D. LOVETT (Somaliland Protectorate) writes: I should like to comment on your expert's answer on the subject of local analgesics for scalds ("Any Questions?" August 7, p. 374). There is, I think, a basic confusion both in the question and its answer. The answer deals with the effect of the various analgesic creams and ointments on the healthy, normal, intact skin. The skin after a burn or scald may be technically unbroken but is certainly damaged to a greater or lesser depth, and this may well facilitate penetration of an ointment. I have experimented with the use of analgesic creams on minor burns and scalds suffered both by myself and by patients and I find the antihistamine type (I have used the Roche product "thephorin") most effective. Not only is there very rapid relief of pain but the course of the injury is altered: erythema disappears, there is no swelling, and blisters do not form. Instead, in second-degree burns, a thin layer of skin, which would without treatment have been raised by blister fluid, becomes dry and hard and separates after a few days leaving regenerated, painless skin beneath. I must emphasize that I have used this ointment only on small burns of first and second degree, and that to be effective it must be applied as soon as possible after the burn is inflicted. It may be argued that an antihistamine ointment is not, strictly speaking, a local analgesic, and this I must concede; but it does, on the other hand, serve the purpose your inquirer had in mind, even if not complying with the strict letter of his question.

Undergraduate Education.—In the *Journal* of August 28 (p. 515) we referred to a survey of the schemes in operation in British medical schools for giving senior students an opportunity to see the work of a general practice. This survey was carried out by Mr. R. W. Heslop and published last year by the British Medical Students' Association, B.M.A. House, London, W.C.1.

Corrections

The paragraph announcing Dr. F. F. Main's appointment as chief medical officer to the Northern Ireland Ministry of Health and Local Government (September 4, p. 603) should have been headed, "New C.M.O. for Northern Ireland," not for "Ulster."

In the memorandum on the intramuscular injection of streptomycin sulphate (September 11, p. 632) the needle used was wrongly stated to have been a No. 1 serum needle. It was, in fact, a No. 1 hypodermic needle (21 S.W.G.).

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